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FILE 'REGISTRY' ENTERED AT 13:27:24 ON 30 SEP 1999
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STRUCTURE FILE UPDATES:   29 SEP  99  HIGHEST RN 242492-07-5
DICTIONARY FILE UPDATES:  29 SEP  99  HIGHEST RN 242492-07-5

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 13, 1999

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

=> e mifepristone/cn

E1            1     MIFEGYNE/CN
E2            1     MIFENTIDINE/CN
E3            1 --> MIFEPRISTONE/CN
E4            1     MIFEPRISTONE-NORETHINDRONE ACETATE-ETHINYLESTRADIOL
MIXT./CN
E5            1     MIFESTONE/CN
E6            1     MIFEX/CN
E7            1     MIFIL PA 20/CN
E8            1     MIFIL PS/CN
E9            1     MIFIL PS 100/CN
E10           1     MIFOBATE/CN
E11           1     MIFORON/CN
E12           1     MIG/CN

=> s e3

L1            1 MIFEPRISTONE/CN

=> d


L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 1999 ACS
RN   84371-65-3  REGISTRY
CN   Estra-4,9-dien-3-one, 11-[4-(dimethylamino)phenyl]-17-hydroxy-17-(1-
     propynyl)-, (11.beta.,17.beta.)- (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   Mifegyne
CN   Mifepristone
CN   Mifestone
CN   R 38486
CN   RU 38486
CN   RU 486
CN   RU 486-6
CN   RU486
FS   STEREOSEARCH
DR   122742-25-0, 83203-42-3
MF   C29 H35 N O2
CI   COM
LC   STN Files:   ADISINSIGHT, AGRICOLA, AIDSLINE, ANABSTR, BEILSTEIN*,
       BIOBUSINESS, BIOSIS, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN,
       CHEMCATS, CIN, CSCHEM, DDFU, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES,
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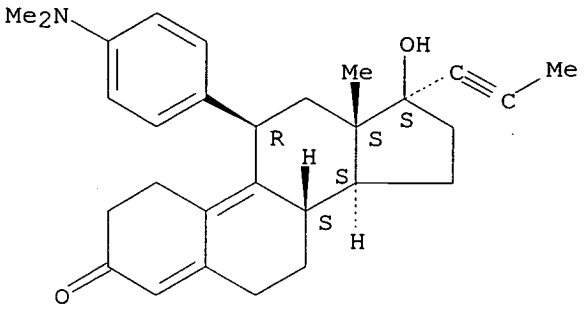
EMBASE, GMELIN*, HSDB*, IPA, MEDLINE, MRCK*, PHAR, PROMT, RTECS*, TOXLINE, TOXLIT, USAN, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: WHO

Absolute stereochemistry.



1391 REFERENCES IN FILE CA (1967 TO DATE)
56 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1395 REFERENCES IN FILE CAPLUS (1967 TO DATE)

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=> e ru 009/cn

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=> e ru 39.009/cn

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E8              1     RU 39130/CN
E9              1     RU 39141/CN
E10             1     RU 39142/CN
E11             1     RU 39171/CN
E12             1     RU 39229/CN

=> s e5

L2              1 "RU 39009"/CN

=> d


L2   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 1999 ACS
RN   84371-63-1  REGISTRY
CN   Estra-4,9-dien-3-one,
11-[4-[2-(dimethylamino)ethoxy]phenyl]-17-hydroxy-17-
     (1-propynyl)-, (11.beta.,17.beta.)- (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   RU 39009
FS   STEREOSEARCH
MF   C31 H39 N O3
LC   STN Files:   CA, CAPLUS, TOXLIT, USPATFULL

Absolute stereochemistry.
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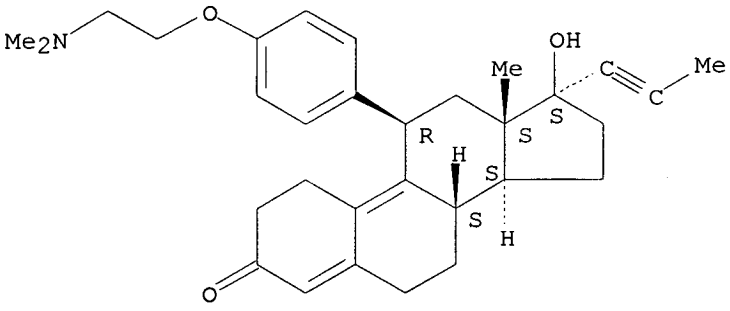


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                6 REFERENCES IN FILE CA (1967 TO DATE)
                6 REFERENCES IN FILE CAPLUS (1967 TO DATE)


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E2              1     RU 004/CN
E3              0 --> RU 044/CN
E4              1     RU 1/CN
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E11           1     RU 106/CN
E12           1     RU 107/CN

=> e ru 43044/cn

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E2            1     RU 43028/CN
E3            1 --> RU 43044/CN
E4            1     RU 43195/CN
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E7            1     RU 43526/CN
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E11           1     RU 43945/CN
E12           1     RU 44/CN

=> s e3

L3            1 "RU 43044"/CN

=> d


L3   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 1999 ACS
RN   136959-96-1  REGISTRY
CN   RU 43044 (9CI)  (CA INDEX NAME)
MF   Unspecified
CI   MAN
SR   CA
LC   STN Files:   CA, CAPLUS, MEDLINE, TOXLINE, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
               6 REFERENCES IN FILE CA (1967 TO DATE)
               6 REFERENCES IN FILE CAPLUS (1967 TO DATE)


=> e ru 44/cn

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E2            1     RU 43945/CN
E3            1 --> RU 44/CN
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E5            1     RU 44403/CN
E6            1     RU 44425/CN
E7            1     RU 44502/CN
E8            1     RU 44570/CN
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E10           1     RU 4462/CN
E11           1     RU 44675/CN
E12           1     RU 44760/CN

=> s e3

L4            1 "RU 44"/CN

=> d
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L4 ANSWER 1 OF 1 REGISTRY COPYRIGHT 1999 ACS
RN 71503-73-6 REGISTRY
CN **RU 44 (9CI)** (CA INDEX NAME)
MF Unspecified
CI MAN
LC STN Files: CA, CAPLUS, TOXLIT

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> file ca,biosis,medline,drugu,embase

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	23.20	23.35

FILE 'CA' ENTERED AT 13:34:40 ON 30 SEP 1999
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FILE 'BIOSIS' ENTERED AT 13:34:40 ON 30 SEP 1999
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FILE 'MEDLINE' ENTERED AT 13:34:40 ON 30 SEP 1999

FILE 'DRUGU' ENTERED AT 13:34:40 ON 30 SEP 1999
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FILE 'EMBASE' ENTERED AT 13:34:40 ON 30 SEP 1999
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=> s l1 or l2 or l3 or l4 or ru486 or ru 486 or mifepristone or ru009 or ru 009 or ru 39009 or ru39009 or ru 9 or ru044 or ru 044 or ru 44 or ru43044 or ru 43044

L5 11834 L1 OR L2 OR L3 OR L4 OR RU486 OR RU 486 OR MIFEPRISTONE OR RU009
OR RU 009 OR RU 39009 OR RU39009 OR RU 9 OR RU044 OR RU 044 OR
RU 44 OR RU43044 OR RU 43044

=> s psychosis or psychot? or antipsycho? or schizo? or alzheim? or cocain?(2a)(addict? or abus?)

L6 463846 PSYCHOSIS OR PSYCHOT? OR ANTIPSYCHO? OR SCHIZO? OR ALZHEIM? OR COCAIN?(2A)(ADDICT? OR ABUS?)

=> s l5 and l6

L7 50 L5 AND L6

=> dup rem l7

PROCESSING COMPLETED FOR L7
L8 36 DUP REM L7 (14 DUPLICATES REMOVED)

=> d 1-36 bib,ab

L8 ANSWER 1 OF 36 CA COPYRIGHT 1999 ACS
AN 130:276766 CA

TI Methods using a glucocorticoid receptor antagonist for treating **psychosis** associated with glucocorticoid-related dysfunction
IN Schatzberg, Alan F.; Belanoff, Joseph K.
PA The Board of Trustees of Leland Stanford Jr. University, USA
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9917779	A1	19990415	WO 1998-US20906	19981005

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9896832	A1	19990427	AU 1998-96832	19981005
PRAI US 1997-60973	19971006			
WO 1998-US20906	19981005			

AB The invention generally pertains to the field of psychiatry. In particular, the invention pertains to the discovery that agents which inhibit the binding of cortisol to its receptors can be used in methods for ameliorating pathologies or conditions assocd. with **psychosis**. These pathologies or conditions include **psychotic** major depression, **schizoaffective** disorders, **Alzheimer**'s Disease and **cocaine addiction**. **Mifepristone**, a potent glucocorticoid receptor antagonist, can be used in these methods. The invention also provides a kit for the amelioration of **psychosis** in a human including a glucocorticoid receptor antagonist and instructional material teaching the indications, dosage and schedule of administration of the glucocorticoid receptor antagonist.

L8 ANSWER 2 OF 36 CA COPYRIGHT 1999 ACS
AN 130:119612 CA
TI Ketoconazole for treatment of **Cocaine addiction**
IN Goeders, Nicholas E.
PA Board of Supervisors of Louisiana State University and Agricultural and Mechanical College, USA
SO U.S., 12 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 5869474	A	19990209	US 1997-857376	19970516

AB Ketoconazole is used for treating **cocaine addiction**. Mammals, including humans, that are chronically **addicted** to **cocaine** are treated with ketoconazole to decrease self-administration of the drug.

L8 ANSWER 3 OF 36 CA COPYRIGHT 1999 ACS
AN 130:510 CA
TI Method and composition for modulating amyloidosis
IN Reiner, Peter B.; Lam, Fred Chiu-lai
PA The University of British Columbia, Can.
SO PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DT Patent

LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9848784	A2	19981105	WO 1998-US8463	19980428
	WO 9848784	A3	19990812		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9872603	A1	19981124	AU 1998-72603	19980428
PRAI	US 1997-847616	19970428			
	WO 1998-US8463	19980428			

AB Methods for modulating amyloid deposition in a subject are described. An effective amt. of at least one ATP-binding cassette (ABC) transporter blocker is administered to a subject, such that modulation of amyloid deposition occurs. Methods also include administering an effective amt. of at least one ABC transporter blocker, or a pharmaceutically acceptable salt thereof, to a subject such that a disease state assocd. with amyloidosis is treated. Packaged pharmaceutical compns. for treating amyloidosis are described. The package includes a container for holding an effective amt. of a pharmaceutical compn. and instructions for using the pharmaceutical compn. for treatment of amyloidosis. The pharmaceutical compn. includes at least one ABC blocker for modulating amyloid deposition in a subject. Methods for identifying agents which modulate amyloid deposition in a subject are also described. An effective amt. of at least one ATP binding cassette (ABC) transporter blocker is administered to an organism, such that modulation of amyloid deposition occurs.

L8 ANSWER 4 OF 36 CA COPYRIGHT 1999 ACS
AN 129:77030 CA
TI Use of **mifepristone** for the treatment of psychoses and addictive behaviors
IN Oberlander, Claude; Piazza, Pier Vincenzo
PA Hoechst Marion Roussel, Fr.; Oberlander, Claude; Piazza, Pier Vincenzo
SO PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9826785	A1	19980625	WO 1997-FR2321	19971217
	W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, GW, HU, ID, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	FR 2757400	A1	19980626	FR 1996-15649	19961219
	AU 9855633	A1	19980715	AU 1998-55633	19971217
	EP 918525	A1	19990602	EP 1997-952079	19971217
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI	FR 1996-15649	19961219			
	WO 1997-FR2321	19971217			

AB The invention discloses the use of **mifepristone** with anti-glucocorticoid activity for prepg. a medicament for the prevention or

treatment of psychoses or addictive behavior, and compns. contg. them.

L8 ANSWER 5 OF 36 CA COPYRIGHT 1999 ACS
AN 129:50105 CA
TI Uses of anti-glucocorticoid compounds for the treatment of psychoses or addictive behaviors
IN Oberlander, Claude; Piazza, Pier Vincenzo
PA Hoechst Marion Roussel, Fr.; Oberlander, Claude; Piazza, Pier Vincenzo
SO PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9826783	A1	19980625	WO 1997-FR2320	19971217
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, GW, HU, ID, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
FR 2757400	A1	19980626	FR 1996-15649	19961219
AU 9855632	A1	19980715	AU 1998-55632	19971217
EP 892641	A1	19990127	EP 1997-952078	19971217
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI FR 1996-15649 19961219
WO 1997-FR2320 19971217
OS MARPAT 129:50105
AB Glucocorticoid antagonists,except **mifepristone**, are used as dopamine type II receptor antagonists to treat **psychotic** or addictive behavior. Thus, 17.beta.-hydroxy-10.beta.-[(4-methylphenyl)methyl]-17.alpha.-(1-propynyl)estra-4,9(11)-dien-3-one considerably reduced the response to morphine in vivo.

L8 ANSWER 6 OF 36 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1998-30878 DRUGU T E S
TI Preliminary report on the treatment of endometriosis with low dose **mifepristone** (**RU 486**).
AU Kettel L M; Murphy A A; Morales A J; Yen S S C
CS Univ.California
LO La Jolla, Cal., USA
SO Am.J.Obstet.Gynecol. (178, No. 6, 1151-56, 1998) 4 Fig. 14 Ref.
CODEN: AJOGAH ISSN: 0002-9378
AV San Diego Fertility Center, 4150 Regents Park Row, Suite 325, La Jolla, CA 92037, U.S.A.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB P.o. low-dose **mifepristone** (MI) induced improvement in pelvic pain and uterine cramping during long-term treatment of 7 patients with pelvic pain due to endometriosis. There was no significant change in the mean degree of surgically visible endometriosis although individual responses varied. Some patients experienced irregular and even heavy bleeding, the latter resolving after treatment with progesterone in oil. Side-effects included a mild increase in liver transaminases, hot flushes and depression. From previous experience with different doses of MI, a higher dose is recommended for continued investigations.

L8 ANSWER 7 OF 36 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD

AN 1998-37493 DRUGU P E V
TI Modulation of androgen and progesterone receptors by phytochemicals in breast cancer cell lines.
AU Rosenberg R S; Grass L; Jenkins D J A; Kendall C W C; Diamandia E P
CS Univ.Toronto
LO Toronto, Ont., Can.
SO Biochem.Biophys.Res.Commun. (248, No. 3, 935-39, 1998) 1 Fig. 3 Tab. 36 Ref.
CODEN: BBRCA9 ISSN: 0006-291X
AV Department of Pathology, Mount Sinai Hospital, 600 University Avenue, Toronto, Ontario, Canada M5G 1X5. (E.P.D.).
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB The breast carcinoma cell lines T-47D and BT-474 were used to investigate the steroid hormone agonist and antagonist activity of apigenin, ascorbate (both Sigma-Chem.), biochanin-A (Indofine), caffeate, caffeine, carotene-beta, catechin, chlorogenate, chlorophylline, daidzin, ellagate, ferulate, gallate (all Sigma-Chem.), genistein, genistate (Indofine), green tea, hesperetin, hesperidin, homocysteine, kaempferol, luteolin, mecobalamin, morin, naringenin, naringin, pyridoxine, quercetin, rutin, rutin-trihydrate, salicylate, saw palmetto (all Sigma-Chem.), syringate, taxifolin, theobromine, theophylline, tocopherol-alpha (last 4 Sigma-Chem.), red wine, coumarate and vanillate. Norgestrel, norgestimate, dihydrotestosterone (both Sigma-Chem.), RU-56187 and **mifepristone** were used.

L8 ANSWER 8 OF 36 BIOSIS COPYRIGHT 1999 BIOSIS DUPLICATE 1
AN 1998:396919 BIOSIS
DN PREV199800396919
TI **Mifepristone**: Auxiliary therapeutic use in cancer and related disorders.
AU Koide, Samuel S. (1)
CS (1) Cent. Biomedical Res., Population Council, 1230 York Ave., New York, NY 10021 USA
SO Journal of Reproductive Medicine, (July, 1998) Vol. 43, No. 7, pp. 551-560.
ISSN: 0024-7758.
DT Article
LA English
AB OBJECTIVE: To evaluate the efficacy of **mifepristone**, a potent antagonist of progesterone and glucorticoids, in the management of cancer and disorders related to reproduction. STUDY DESIGN: Reports describing clinical trials of **mifepristone** treatment of leiomyoma, breast cancer, endometriosis and meningioma were received. **Mifepristone** is a potent antagonist of progesterone and glucocorticoids. It is an effective contraceptive and abortifacient and in addition has been used in the management of diseases associated with pregnancy and adrenal cortical function. Results of the clinical trials show that it has beneficial and palliative value in some cases. **Mifepristone** may be used as an adjuvant therapeutic agent in cases of unresectable meningioma and leiomyoma that are refractory to chemotherapy, endocrine treatment or irradiation. In extensive endometriosis, **mifepristone** is indicated for intractable pain, although its effect on the lesions will be minimal. In the management of unresectable and metastatic breast cancer, **mifepristone** may be considered after a course of chemotherapy and/or irradiation and only in combination with another agent. In Cushing's syndrome **mifepristone** may be used to treat the

undesirable sequelae of excessive cortisol production-e.g., **psychosis**. It will have minimal or no effect on the lesions of the adrenal or pituitary. To adverse effects of the long-term use of **mifepristone** are slight to moderate and reflect antiglucocorticoid effects. During treatment with **mifepristone** one should be aware of the possibility that the patient will develop Addisonian-like syndrome in the face of elevated blood ACTH and cortisol levels. RESULTS: Leiomyoma treated with 25 or 50 mg/d of **mifepristone** underwent a 25-49% reduction in tumor size. Treatment of endometriosis with a daily dose of 50 or 100 mg or **mifepristone** alleviated pelvic pain and uterine cramps and induced about 55% regression of the lesions. Treatment of metastatic breast cancer with 200 or 400 mg/d of **mifepristone** resulted in a partial response. Unresectable meningioma treated with 200 or 400 mg/d of **mifepristone** produced objective improvement in about 25% of subjects. CONCLUSION: **Mifepristone** is beneficial as adjuvant treatment in the management of unresectable, hormone-dependent tumors and disorders of the female reproductive system that are refractory to chemotherapy and irradiation.

L8 ANSWER 9 OF 36 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 1999012137 EMBASE
TI [News from drug research and drug development].
NEUES AUS ARZNEIMITTELFORSCHUNG UND -ENTWICKLUNG.
SO Deutsche Apotheker Zeitung, (17 Dec 1998) 138/51-52 SUPPL. (4-10).
ISSN: 0011-9857 CODEN: DAZEA2
CY Germany
DT Journal; (Short Survey)
FS 030 Pharmacology
037 Drug Literature Index
LA German

L8 ANSWER 10 OF 36 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1998-15378 DRUGU P
TI The genetic variant A of human alpha 1-acid glycoprotein limits the blood to brain transfer of drugs it binds.
AU Jolliet Riant P; Boukef M F; Duche J C; Simon N; Tillement J P
LO Creteil, Fr.
SO Life Sci. (62, No. 14, PL219-26, 1998) 2 Tab. 22 Ref.
CODEN: LIFSAK ISSN: 0024-3205
AV Service de Pharmacologie, Faculte de Medecine de Paris XII, 8 rue du General Sarrail, F-94010 Creteil, France. (e-mail: jolliet@univ-paris12.fr).
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB The effects of alpha-1 acid glycoprotein (AAG) and its components, A and F1/S variants on the brain transfer of disopyramide, imipramine, methadone, **mifepristone**, chlorpromazine and propranolol (all i.v. bolus) were studied in rats. The brain transfers of the drugs almost exclusively bound to A variant, imipramine, disopyramide and methadone were reduced when bound to AAG. The brain transfer of the 2 drugs simultaneously bound to A and F1/S variants (chlorpromazine and propranolol) were reduced when associated to the variant A, but to a lesser extent. AAG binding reduced brain transfer when the A variant is mainly and almost exclusively involved in this binding. On the contrary, the entire fraction of the tested drugs when bound exclusively or partly to the mixture F1/S is available for transfer into the brain.

L8 ANSWER 11 OF 36 BIOSIS COPYRIGHT 1999 BIOSIS DUPLICATE 2
AN 1997:306630 BIOSIS

DN PREV199799614433
TI Protection against oxidative stress-induced neuronal cell death. A novel role for **RU486**.
AU Behl, Christian (1); Trapp, Thorsten; Skutella, Thomas; Holsboer, Florian
CS (1) Max Planck Inst. Psychiatry, Clinical Inst., Kraepelinstrasse 10, 80804 Munich Germany
SO European Journal of Neuroscience, (1997) Vol. 9, No. 5, pp. 912-920. ISSN: 0953-816X.
DT Article
LA English
AB Free radicals and oxidative stress-induced neuronal cell death have been implicated in a variety of neurological disorders. Therefore, neuroprotection is of primary interest in basic and preclinical neuroscience. Here it is shown that **RU486** (**mifepristone**), a potent antagonist of progesterone and glucocorticoid receptors, protects rat primary hippocampal neurons, clonal mouse hippocampal cells and organotypic hippocampal slice cultures against oxidative stress-induced neuronal cell death. 10-5 M **RU486** prevents intracellular peroxide accumulation and cell death induced by amyloid beta protein, hydrogen peroxide and glutamate, neurotoxins that have been implicated in certain neurodegenerative disorders, including **Alzheimer**'s disease. **RU486** has a significant protective effect that is independent of the presence and activation of glucocorticoid or progesterone receptors. The neuroprotective activity of this well-studied drug may have an impact on therapeutic interventions for neurodegenerative conditions which involve peroxidation processes, such as stroke and **Alzheimer**'s disease.

L8 ANSWER 12 OF 36 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 97209154 EMBASE
DN 1997209154
TI Hormonal interventions with psychopharmacological potential: An overview.
AU Halbreich U.
CS Dr. U. Halbreich, State University of New York, SUNY Clinical Center, 462 Grider Street, Buffalo, NY 14215, United States
SO Psychopharmacology Bulletin, (1997) 33/2 (281-286).
Refs: 69
ISSN: 0048-5764 CODEN: PSYBB
CY United States
DT Journal; General Review
FS 030 Pharmacology
032 Psychiatry
037 Drug Literature Index
LA English
SL English
AB The better understanding of how hormones modulate cognition and behavior is associated with the application of hormones as **psychotropic** medications. Several natural and synthetic hormones are used as adjuncts to antidepressant medications or as treatments in their own right. We discuss pharmacotherapeutical aspects of estrogen, thyroid hormones, cortisol suppressors, end melatonin as examples of current trends in the field. In addition to the putative roles of these hormones in the treatment of effective disorders, estrogen might also be used as a cognition-enhancer, and both estrogen and thyroid hormones might have roles as mood stabilizers. The psychofropic effects of melatonin have recently received significant attention, but the exact role of that hormone still needs to be clarified.

L8 ANSWER 13 OF 36 CA COPYRIGHT 1999 ACS DUPLICATE 3
AN 126:55042 CA
TI Glucocorticoids enhance oxidative stress-induced cell death in hippocampal

neurons in vitro
AU Behl, Christian; Lezoulac'h, Frank; Trapp, Thorsten; Widmann, Martina; Skutella, Thomas; Holsboer, Florian
CS Max Planck Institute of Psychiatry, Clinical Institute, Munich, 80804, Germany
SO Endocrinology (1997), 138(1), 101-106
CODEN: ENDOAO; ISSN: 0013-7227
PB Endocrine Society
DT Journal
LA English
AB In patients with **Alzheimer**'s disease, hippocampal cells are among the first neuronal cells of the brain to degenerate. Both rat primary hippocampal neurons and cells of the clonal mouse hippocampal cell line HT22 express endogenous functional glucocorticoid receptors (GRs), as shown by transient transfection of cells with a luciferase reporter plasmid contg. GR-responsive elements. The influence of activated GRs on oxidative stress-induced neuronal cell death in vitro was investigated employing these hippocampal model systems. Two oxidative stressors were investigated, the free radical-inducing **Alzheimers**'s disease-assocd. amyloid .beta.-protein, which is toxic to hippocampal neurons, and the excitatory amino acid glutamate, which induces oxidative cell death in HT22 cells via an increase in intracellular peroxides. Cellular viability was assessed with the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-tetrazolium bromide test and trypan exclusion staining, followed by microscopical cell counting. Glucocorticoids strongly increased the vulnerability of the hippocampal cells to amyloid .beta.-protein and glutamate. This increase could be blocked by the specific GR antagonist **RU 486**. Changes in hippocampal GR homeostasis and regulation may render hippocampal neurons more vulnerable to oxidative stress-induced neuronal degeneration.

L8 ANSWER 14 OF 36 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 1998006753 EMBASE
TI Anticortisols (**RU-486**) can help many, says developer.
AU Blank C.
SO Drug Topics, (1997) 141/23 (30-32).
ISSN: 0012-6616 CODEN: DGTNA7
CY United States
DT Journal; (Short Survey)
FS 003 Endocrinology
006 Internal Medicine
037 Drug Literature Index
LA English

L8 ANSWER 15 OF 36 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 96216671 EMBASE
DN 1996216671
TI Is there a role for estrogen replacement therapy in the prevention and treatment of dementia?.
AU Birge S.J.; Kuller L.H.
CS Div. of Geriatrics and Gerontology, Washington Univ. School of Medicine, 216 S. Kingshighway Blvd.,St. Louis, MO 63110, United States
SO Journal of the American Geriatrics Society, (1996) 44/7 (865-870+878-880).
ISSN: 0002-8614 CODEN: JAGSAF
CY United States
DT Journal; General Review
FS 003 Endocrinology
008 Neurology and Neurosurgery
020 Gerontology and Geriatrics
037 Drug Literature Index
LA English

SL English
AB Studies in experimental animal models provide a convincing rationale for a role for ERT in the treatment and prevention of dementia. These studies establish the role of estrogen in the regeneration and preservation of neuronal elements within the CNS that are analogous to those regions of the brain most sensitive to the neurodegenerative changes associated with AD. Furthermore, behavioral studies in these animals establish a correlation between the hormone dependent changes in the neuronal architecture and learning and memory. However, extrapolation of these studies to postmenopausal women must be done with caution. Surgical and natural loss of ovarian function does not result in a clinically relevant decline in cognitive function over the short term (1 to 2 decades) or ever in some women. The modest changes that are observed may relate to the hormone's effect on neurotransmitter levels or their receptors. Although Singh et al. noted changes in neurotransmitter concentrations 5 weeks after ovariectomy, changes in cognitive performance in their rat model did not become significant until 28 week after ovariectomy-the equivalent of approximately 2 decades of human life. Except for the familial forms of the disease, AD is rarely seen in the first 2 decades after the menopause.

However, by the third decade after the menopause, 50% of women can be expected to manifest the histopathological changes of AD. Approximately half of these women are without clinical evidence of disease. Thus, the neurodegenerative process of AD probably precedes by many years the age of onset of the disease. We do not know what factors contribute to the selective neuronal injury which, over time, eventually leads to the neuronal loss and reduced synaptic density that result in the cognitive impairment of AD. At this time we can only speculate as to estrogen's role in modifying this process. Data from experimental animal models suggest that estrogen deficiency would selectively increase the vulnerability of estrogen-responsive neural elements, for example, the cholinergic neurons of the basal forebrain and hippocampus-a vulnerability mediated perhaps by the reduced expression of neurotrophic factors, decreased clearance of the amyloid protein, and/or reduced cerebral blood flow that are associated with estrogen deficiency. The brain's ability to adapt to the neuronal loss by stimulating axonal and synaptic regeneration would also be impaired by estrogen deficiency as suggested by estrogen's ability to restore the synaptic density of lesioned brains of ovariectomized animals.

Thus, estrogen deficiency, like the apolipoprotein E4 allele, can be considered not a cause of AD but one of perhaps several factors modifying the neuronal injury and loss leading to AD. The limited epidemiologic data and intervention trials currently available are consistent with this interpretation. Because of the urgency and enormity of the problem of dementia in our aging society, there would now appear to be sufficient reason to allocate the resources needed to conduct the appropriate clinical trials to determine estrogen's efficacy in both the treatment and prevention of this devastating condition. These trials are needed so that women and their physicians can adequately weigh the risks and benefits of hormone replacement for the treatment and, more importantly, the prevention of dementia.

L8 ANSWER 16 OF 36 EMBASE
AN 97004460 EMBASE
DN 1997004460
TI Treatment of tumors of the brain.

AU Krouwer H.G.; Meyer G.A.
CS Dr. H.G. Krouwer, Department of Neurology, MCW at Froedtert, 9200 W. Wisconsin Ave, Milwaukee, WI 53226, United States
SO Wisconsin Medical Journal, (1996) 95/12 (852-859).
ISSN: 0043-6542 CODEN: WMJOA7
CY United States
DT Journal; General Review
FS 006 Internal Medicine
008 Neurology and Neurosurgery
016 Cancer
037 Drug Literature Index
038 Adverse Reactions Titles
LA English

L8 ANSWER 17 OF 36 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1996:493957 BIOSIS
DN PREV199699216313
TI **RU486** regulates beta-APP processing.
AU Lam, F.; Reiner, P. B.
CS Kinsmen Lab. Neurol. Res., Univ. B.C., Vancouver, BC V6T 1Z3 Canada
SO Society for Neuroscience Abstracts, (1996) Vol. 22, No. 1-3, pp. 190.
Meeting Info.: 26th Annual Meeting of the Society for Neuroscience Washington, D.C., USA November 16-21, 1996
ISSN: 0190-5295.
DT Conference
LA English

L8 ANSWER 18 OF 36 CA COPYRIGHT 1999 ACS DUPLICATE 4
AN 124:220844 CA
TI Monoamine oxidase B expression is selectively regulated by dexamethasone in cultured rat astrocytes
AU Carlo, Pia; Violani, Elisabetta; Rio, Meris Del; Olasmaa, Marjut; Santagati, Sabrina; Maggi, Adriana; Picotti, Giovanni B.
CS Institute of Pharmacology, School of Medicine, University of Genoa, Viale Benedetto XV 2, Genoa, I-16132, Italy
SO Brain Res. (1996), 711(1,2), 175-83
CODEN: BRREAP; ISSN: 0006-8993
DT Journal
LA English
AB The influence of dexamethasone on monoamine oxidase (MAO) A and B expression and activity was investigated in primary cultures of rat type 1 astrocytes cultured under serum free, defined conditions. Dexamethasone treatment resulted in a dose- and time-dependent induction of MAO-B, but not of MAO-A, activity. The selective MAO-B increase was substantially reduced by the antagonist **RU 486**, thus suggesting a glucocorticoid receptor-mediated action of the hormone. Kinetic anal. showed an increase in Vmax of MAO-B with no change in apparent Km. The dexamethasone-induced selective rise in MAO-B activity appeared to be due to enhanced enzyme synthesis, since MAO-B mRNA was markedly increased by dexamethasone treatment and the recovery of MAO-B activity after its irreversible inhibition by deprenyl was more pronounced in the presence than in the absence of the hormone. Furthermore, the dexamethasone effect was abolished by the protein synthesis inhibitors actinomycin D or cycloheximide. The present study demonstrates that dexamethasone is able to selectively induce MAO-B in type 1 astrocytes and leads to speculation of a possible role for glucocorticoids in the increase in brain MAO-B assocd. with neurodegenerative disorders, such as Parkinson's and **Alzheimer**'s diseases.

L8 ANSWER 19 OF 36 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 96072917 EMBASE
DN 1996072917
TI Premenstrual and postpartum mood disorders.

AU Parry B.L.
CS Department of Psychiatry 0804, University of California, 9500 Gilman Drive,La Jolla, CA 92093-0804, United States
SO Current Opinion in Psychiatry, (1996) 9/1 (11-16).
ISSN: 0951-7367 CODEN: COPPE8
CY United Kingdom
DT Journal; General Review
FS 010 Obstetrics and Gynecology
032 Psychiatry
037 Drug Literature Index
038 Adverse Reactions Titles
LA English
SL English
AB Premenstrual dysphoric disorder has been categorized under mood disorders in the DSM-IV as depression, not otherwise specified, although the research diagnostic criteria for premenstrual dysphoric disorder are listed in the appendix. Postpartum depression and **psychosis** have been categorized under mood disorders in the DSM-IV as course modifiers. Support for the categorization of these illnesses as mood disorders is increasing.

L8 ANSWER 20 OF 36 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1995-16867 DRUGU P T E
TI Corticosteroid receptor antagonists: a current perspective.
AU Sutanto W; Kloet E R de
CS Sylvius; Bio-Pharm.Sci.
LO Leiden, Neth.
SO ; Pharm.World Sci. (17, No. 2, 31-41, 1995) 4 Fig. 2 Tab. 143 Ref.
CODEN: ; PWSC
AV Divisions of Pharmacology and Medical Pharmacology, Centre for Bio-Pharmaceutical Sciences, Sylvius Laboratories, P.O. Box 9503, 2300 RA, Leiden the Netherlands.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB Conventional and novel ligands which bind to glucocorticoid or mineralocorticoid receptors are discussed in this review in terms of their pharmacology and clinical applications. The structure of anti-mineralocorticoids and anti-glucocorticoids determine their activities. At the receptor level selective antagonist binding can be changed by alteration of the ligands which interact with the receptor. Anti-glucocorticoids and anti-mineralocorticoids have been clinically used for the treatment of hyperaldosteronism, congestive cardiac failure, essential hypertension, precocious puberty, obesity, infertility, depression and many others.

L8 ANSWER 21 OF 36 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 94301405 EMBASE
DN 1994301405
TI [New orientations of psychopharmacology in depressive states].
NOUVELLES ORIENTATIONS DE LA PSYCHOPHARMACOLOGIE DES ETATS DEPRESSIFS.
AU Schulz P.; Aubry J.-M.; Schaad N.
CS Div. de Psychopharmacologie Clinique,1225 Chene-Bourg, Switzerland
SO Medecine et Hygiene, (1994) 52/2040 (1885-1886+1888-1889).
ISSN: 0025-6749 CODEN: MEHGAB
CY Switzerland
DT Journal; (Short Survey)
FS 002 Physiology
032 Psychiatry
030 Pharmacology
037 Drug Literature Index
LA French
SL English; French

AB Drug treatment of psychiatric disorders has changed recently, and it is becoming necessary for clinicians to differentiate new **psychotropic** agents on the basis of their pharmacological actions on receptors, membrane transporters, cytoplasmic enzymes and second messengers that these drugs influence. This is illustrated by the example of drug treatment of depression. This evolution complicates postgraduate training of clinicians, but will hopefully lead to better medication with less side effects.

L8 ANSWER 22 OF 36 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 95012346 EMBASE
DN 1995012346
TI Transplacental passage and feto-placental metabolism of drugs: Study design, therapeutic contribution and implications.
AU Bourget P.; Roulot C.; Fernandez H.
CS Service de Pharmacie Clinique, Laboratoire de Toxicologie, Hopital Antoine Beclere, 157 Rue de la Porte de Trivaux,92141 Clamart Cedex, France
SO Therapie, (1994) 49/6 (481-497).
ISSN: 0040-5957 CODEN: THERAP
CY France
DT Journal; General Review
FS 010 Obstetrics and Gynecology
030 Pharmacology
037 Drug Literature Index
LA French
SL English; French
AB Pregnancy is a specific dynamic state and the potential usefulness of caring for a fetal and/or adjacent disorder by treating the mother is now well established. Pregnant women being excluded from the investigational field of clinical trials, only few studies exist concerning evaluation of the pergestational metabolism or transplacental transfer (TPT) of drugs. Questions are extensive and complex. Does TPT occur at a given gestational age (GA), in the context of a particular type of pathology, when a drug is administered by a certain dosage regimen? If this is the case, what is the rapidity of penetration of the products of conception by the drug (bearing in mind its physical-chemical characteristics)? Need harmful adverse effects on the child be feared? Is such penetration desirable, of no consequence or dangerous ? Does the possibility exist of accumulation in the placenta, fetal tissue or amniotic fluid? Should such findings modify the therapeutic regimens of drugs given to expectant mothers? After dealing with the ethical and physlological context in which such research is undertaken, the authors review methods for the study of TPT developed both in vitro and in vivo. The current review covers the period between 1972 and 1993. Exchange mechanisms are complicated and models developed in vitro only partially reflect the actual equilibria which develop. These include 1) the perfused cotyledon model, which while simple, elegant and inexpensive, offers only a localized and fixed view of pregnancy; 2) the necessary study, using microsomes, of placental metabolic capacity (enzyme cartography). In vivo study of TPT is based upon various multicompartmental pharmacokinetic models, some of which have been relatively validated in animals. The simplest indicator for the in vivo evaluation of TPT of a drug in the human species is determination of a feto-maternal blood concentrations ratio (usually performed at the time of separation). The usefulness and limitations of this parameter are controversial, and it would seem preferable to associate it with a kinetic profile of variations in blood concentrations established in the mother.

Any extrapolation of a single result to fetal and adjacent tissues must be done with the greatest caution. Study of the TPT of therapeutically useful agents Is essential to the understanding of their metabolism and is a prerequisite to the use of medications during pregnancy, bearing in mind that any such use must always be with the greatest care and with extremely well-founded indications.

L8 ANSWER 23 OF 36 CA COPYRIGHT 1999 ACS
AN 120:184649 CA
TI Mutated steroid hormone receptors and their use in identification of receptor agonists/antagonists and as molecular switch in transgenic plants and animals and in gene therapy
IN Vegeto, Elisabetta; McDonnel, Donald P.; O'Malley, Bert W.; Schrader, William T.; Tsai, Ming Jer
PA Baylor College of Medicine, USA
SO PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9323431	A1	19931125	WO 1993-US4399	19930511
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5364791	A	19941115	US 1992-882771	19920514
AU 9342417	A1	19931213	AU 1993-42417	19930511
AU 685054	B2	19980115		
JP 07509694	T2	19951026	JP 1993-503676	19930511
EP 745121	A1	19961204	EP 1993-911198	19930511
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
US 5935934	A	19990810	US 1995-454418	19950530
US 5874534	A	19990223	US 1995-479846	19950606
AU 9860651	A1	19980702	AU 1998-60651	19980403

PRAI US 1992-882771 19920514
US 1992-939246 19920902
WO 1993-US4399 19930511

AB Steroid hormone receptor analogs are described which analogs are useful in studying agonist/antagonist activity of ligands or in detg. endogenous ligands for steroid hormone receptors. Plasmids contg. steroid hormone receptor analog genes and cells transfected with those plasmids are provided. The receptor analogs may be used in a mol. switch for regulating gene expression. By site-directed mutagenesis cDNA for the human progesterone receptor was altered. One clone produced a C-terminal truncated receptor which was activated by RU38486, but not by progesterone or the agonist R5020. RU38486 acted as an agonist for this receptor analog in yeast and in mammalian cells.

L8 ANSWER 24 OF 36 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 93212287 EMBASE
DN 1993212287
TI 'Hurry up and wait' characterizes **RU486** status today.
AU Jenks S.
SO Journal of the National Cancer Institute, (1993) 85/14 (1110-1111).
ISSN: 0027-8874 CODEN: JNCIAM
CY United States
DT Journal; Note
FS 006 Internal Medicine

010 Obstetrics and Gynecology
016 Cancer
037 Drug Literature Index
LA English

L8 ANSWER 25 OF 36 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1993-44162 DRUGU P E
TI Evidence for Differences in the Binding of Drugs to the Two Main Genetic Variants of Human Alpha1-Acid Glycoprotein.
AU Herve F; Gomas E; Duche J C; Tillement J P
LO Paris, France
SO Br.J.Clin.Pharmacol. (36, No. 3, 241-49, 1993) 2 Fig. 3 Tab. 32 Ref.
CODEN: BCPHBM ISSN: 0306-5251
AV Laboratoire Hospitalo-Universitaire de Pharmacologie, Hopital Intercommunal de Creteil, Faculte de Medecine de Paris XII, 40 avenue de Verdum, 94010 Creteil Cedex, France.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB Imipramine HCl (IM; CIBA-Geigy), warfarin (WA; Sigma-Chem.) and **mifepristone** (MI; Roussel-UCLAF) were bound to differing extents by the A and F1 + S genetic variants of human alpha1-acid-glycoprotein (AAG), obtained by fractionation of a commercial AAG preparation. The A variant bound IM with high affinity to 1 site/molecule, while the mixed F1 + S fraction had a relatively low affinity for IM, but high affinities for WA and MI. Results obtained with AAG from F1/A and S/A phenotypic individuals, and with unfractionated Cohn fraction VI, were consistent with data from the separated fractions. The genetic polymorphism of AAG may be a source of interindividual variation in plasma drug-binding capacity.

L8 ANSWER 26 OF 36 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTDDUPLICATE 5
AN 1993-29824 DRUGU B T S E
TI Aspects of Medical Therapy of Neuroendocrine Disorders.
AU Lely A J van der
LO Rotterdam, Netherlands
SO Pharm.World Sci. (15, No. 2, 89-90, 1993) 6 Ref.
CODEN: PWSCED
AV University Hospital Rotterdam-Dijkzigt, Dr. Molewaterplein 40, 3015 GD Rotterdam, The Netherlands.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB Studies on aspects of the treatment of acromegaly, prolactinomas and Cushing's syndrome are described. Octreotide (OC), bromocriptine (BR) and thyroliberin inhibited the release of GH in a study of elderly patients with acromegaly. P.o. BR + s.c. OC had an additive effect in lowering GH levels in a study of 51 acromegalic patients. OC increased GH in human GH-secreting pituitary adenoma cells probably by increasing GH mRNA, thus accounting for the lack of tumor shrinkage. CV-205-502 (quinagolide) reduced prolactin (PL) levels in a study of 12 macroprolactinomas patients and 8 with PL-secreting tumors. Side-effects were mild and transient. **Mifepristone** (MI) induced a rapid glucocorticoid receptor-blocking response and reversed **psychosis** in a study of 4 patients with adrenal cancer, Cushing's syndrome and/or lung cancer.

L8 ANSWER 27 OF 36 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1992-40953 DRUGU T E

TI **RU486** in Depression.
AU Krishnan K R R; Reed D; Wilson W H; Saunders W B; Ritchie J C; Nemeroff C
B
LO Durham, North Carolina, Atlanta, Georgia, United States
SO Prog.NeuroPsychopharmacol.Biol.Psychiatry (16, No. 6, 913-20, 1992) 2 Fig. 2 Tab. 11 Ref.
CODEN: PNPPD7 ISSN: 0278-5846
AV Department of Psychiatry, Box 3215, Duke University Medical Center, Durham, NC27710, U.S.A. (7 authors).
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB P.o. **mifepristone** (**RU-486**, Roussel-UCLAF) produced an increase in hypothalamo- pituitary- adrenal (HPA) activity in a placebo-controlled study in 7 patients with major depression, as indicated by hydrocortisone and ACTH levels. 3 Patients were nonsuppressors in the dexamethasone suppression test (DST). All 7 healthy controls were suppressors. The results support the hypothesis that there is increased suprahypophyseal stimulation of the anterior pituitary in depressed patients.

L8 ANSWER 28 OF 36 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 92155605 EMBASE
DN 1992155605
TI Feminist group plans 'economic pressure campaign' for access to **RU 486**.
AU Jenks S.
SO Journal of the National Cancer Institute, (1992) 84/8 (562-563).
ISSN: 0027-8874 CODEN: JNCIAM
CY United States
DT Journal; Note
FS 010 Obstetrics and Gynecology
016 Cancer
037 Drug Literature Index
LA English

L8 ANSWER 29 OF 36 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1992-16029 DRUGU P B E
TI Towards Genomic Pharmacology: From Membranal to Nuclear Receptors.
AU Laduron P M
CS Rhone-Poulenc
LO Vitry-sur-Seine, France
SO Adv.Drug Res. (22, 107-48, 1992) 5 Fig. 1 Tab. 185 Ref.
CODEN: ADRRAN ISSN: 0065-2490
AV Research Centre, Rhone-Poulenc Rorer, 13 Quai Jules Guesde, F-94403 Vitry-sur-Seine Cedex, France.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB Genomic pharmacology is reviewed with reference to gene expression regulation and drug-induced changes in gene expression. The fundamental control point of gene expression is RNA transcription regulation which is compared in prokaryote and eukaryote organisms. **Psychotropics** (e.g. haloperidol, SCH-23390, bromocriptine, amphetamine, cocaine, imipramine, nortriptyline, fluvoxamine, fluoxetine, tranylcypromine, reserpine) modify enzyme mRNA levels. The nucleus as a drug target is discussed with reference to the actions of antihormones (e.g. flutamide, tamoxifen, spironolactone, **RU-486** (**mifepristone**), cortexolone, 4-hydroxytamoxifen and retinoic acid) and cytostatics (e.g. adriamycin, daunomycin, cyclophosphamide and methotrexate) which are the only drugs that interact with DNA.

L8 ANSWER 30 OF 36 BIOSIS COPYRIGHT 1999 BIOSIS DUPLICATE 6
AN 1991:123505 BIOSIS
DN BR40:55190
TI RAPID REVERSAL OF ACUTE **PSYCHOSIS** IN THE CUSHING SYNDROME WITH THE CORTISOL-RECEPTOR ANTAGONIST **MIFEPRISTONE RU-486**.
AU VAN DER LELY A-J; FOEKEN K; VAN DER MAST R C; LAMBERTS S W J
CS DEP. MED., UNIV. HOSP. DIJKZIGT, 40 DR. MOLEWATERPLEIN, 3015 GD ROTTERDAM, NETHERLANDS.
SO Ann. Intern. Med., (1991) 114 (2), 143-144.
CODEN: AIMEAS. ISSN: 0003-4819.
FS BR; OLD
LA English

L8 ANSWER 31 OF 36 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 90372681 EMBASE
DN 1990372681
TI [New in drug therapy].
NOVIDADES DA TERAPEUTICA.
AU Barata da Silveira M.A.
CS Brazil
SO Revista Brasileira de Medicina, (1990) 47/8 (336-342).
ISSN: 0034-7264 CODEN: RBMEAU
CY Brazil
DT Journal; (Short Survey)
FS 006 Internal Medicine
012 Ophthalmology
018 Cardiovascular Diseases and Cardiovascular Surgery
025 Hematology
026 Immunology, Serology and Transplantation
048 Gastroenterology
037 Drug Literature Index
LA Portuguese
SL English

L8 ANSWER 32 OF 36 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1990-11851 DRUGU P
TI Use of 1-Anilino-8-Naphthalene Sulfonate as a Fluorescent Probe in the Investigation of Drug Interactions with Human alpha-1-Acid Glycoprotein and Serum Albumin.
AU Essassi D; Zini R; Tillement J P
LO Creteil, France
SO J.Pharm.Sci. (79, No. 1, 9-13, 1990) 4 Fig. 2 Tab. 32 Ref.
CODEN: JPMSAE ISSN: 0022-3549
AV Faculte de Medecine de Paris XII, Departement de Pharmacologie, 8 rue du General Sarrail, 94010 Creteil Cedex, France.
LA English
DT Journal
FA AB; LA; CT; MPC
FS Literature
AB Using 1-anilino-8-naphthalene sulfonate (ANS, Merck) as fluorescent probe, binding affinities for human alpha-1-acid glycoprotein (AAG) were determined for promethazine, **mifepristone**, disopyramide (Roussel- Uclaf), binedaline (Cassenne), bupivacaine, lidocaine (Bellon), mianserin (Organon), indomethacin (Merck-Chibret), chlorpromazine (Specia), amitriptyline, diazepam (Roche), ticlopidine, propisomide (Sanofi), pipequaline (Rhone-Poulenc), propranolol (ICI-Pharma), clomipramine, imipramine, desipramine (CIBA-Geigy), pindolol (Sandoz), quinidine (Sarget), tolbutamide (Hoechst), erythromycin (Abbott), nortriptyline (Squibb), loxapine (Lederle), haloperidol (Theraplix) and auramine O (Mallet-Sigma). Binding of 14C-pipequaline to HSA was inhibited by diazepam, azapropazone, and ibuprofen but increased by

warfarin.

L8 ANSWER 33 OF 36 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1990-17891 DRUGU P E
TI Effects of Glucocorticoid Antagonism With **RU 486** on Pituitary-Adrenal Function in Patients With Major Depression: Time-Dependent Enhancement of Plasma ACTH Secretion.
AU Kling M A; Whitfield H J Jr; Brandt H A; Demitrack M A; Kalogeras K; Geracioti T D
LO Bethesda, Maryland, Cleveland, Ohio, United States
SO Psychopharmacol.Bull. (25, No. 3, 466-72, 1989) 4 Fig. 14 Ref.
CODEN: PSYBB9 ISSN: 0048-5764
AV Clinical Neuroendocrinology Branch, NIMH, NIH, Building 10, Room 3S-231, Bethesda, MD 20892, U.S.A. (10 authors).
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB In a double-blind, placebo-controlled clinical trial, the pituitary responses to p.o. RU-846 (RU; **Mifepristone** Roussel-UCLAF) were investigated in 8 patients with major depression and in 8 healthy subjects. Results showed that RU produced a robust increase in plasma ACTH and cortisol secretion in both control subjects and in depressed patients. 7 Patients also received ovine corticoliberin stimulation testing.

L8 ANSWER 34 OF 36 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1988-51641 DRUGU P E
TI The Effects of Progesterone Receptor Blockade in the Luteal Phase of Normal Fertile Women.
AU Li T C; Dockery P; Thomas P; Rogers A W; Lenton E A; Cooke I D
CS Roussel-Uclaf
LO Uxbridge, United Kingdom
SO Fertil.Steril. (50, No. 5, 732-42, 1988) 3 Fig. 3 Tab. 25 Ref.
CODEN: FESTAS ISSN: 0015-0282
AV Jessop Hospital for Women, Sheffield, S3 7RE, England.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB RU-38486 (**RU-486**, **Mifepristone**, Roussel-Uclaf) inhibited glandular secretory activity, accelerated degenerative changes and induced vascular changes in 30 normal fertile women when it was given in the luteal phase of their menstrual cycle. **RU-486** also increased stromal but not glandular mitotic activity and did not affect the predecidual reaction. Menstrual induction and changes in hypothalamic function after **RU-486** occurred independently of luteolysis. Menstrual induction was significantly related to the dose given and the day of administration of **RU-486**. Mood changes (irritability, depression) were related to the day of administration. Other side-effects included thirst.

L8 ANSWER 35 OF 36 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1988-41783 DRUGU P E
TI Cortisol Response of Bipolar Patients Receiving an Antiglucorticoid.
AU ---
LO Germany,West
SO Psychopharmacology(Berlin) (96, Suppl., 264, 1988)
CODEN: PSCHDL ISSN: 0033-3158
AV No Reprint Address.
LA English
DT Journal
FA AB; LA; CT

FS Literature
AB In normal subjects, administration of the antiglucocorticoid, **RU -486 (mifepristone)** induced a disinhibition of the pituitary - adrenal axis and antagonized the ACTH inhibitory effect of dexamethasone. When administered at midnight or 10.00 hr, the increase in plasma cortisol, ACTH and beta-endorphin occurred only during the early morning peak. In bipolar patients, the increase in cortisol secretion was greater than that in controls. The best time to discriminate patients from controls was 15.00 hr. (congress abstract).

L8 ANSWER 36 OF 36 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1986-12085 DRUGU P E
TI Afternoon Increase in Plasma Cortisol in Depressed Patients Receiving an Antiglucocorticosteroid in the Morning.
AU Ammar S; Allilaire J F; Lecrubier Y; Widlocher D; Baulieu E E
LO Paris, France
SO Am.J.Psychiatry (143, No. 1, 129-30, 1986) 5 Ref.
CODEN: AJPSAO ISSN: 0002-953X
AV No Reprint Address.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB Afternoon plasma cortisol levels after dosing with **RU-486** in the morning, were higher in 5 patients with acute depression and melancholia than in 4 previously-reported volunteers. The results suggest that **RU-486** might help to reveal a neurohormonal deficit in endogenous depression and may provide a way to attribute diagnostic and pathopysiological importance to cortisol measurements in psychiatric patients.

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=> s (glucocorticoid? or cortisol or hydrocortisone)(2a)(antagonist? or
block? or inhibit?) or antiglucocorticoid? or anti-glucocorticoid

   4 FILES SEARCHED...
L9       17076 (GLUCOCORTICOID? OR CORTISOL OR
HYDROCORTISONE)(2A)(ANTAGONIST?
               OR BLOCK? OR INHIBIT?) OR ANTIGLUCOCORTICOID? OR
ANTI-GLUCOCORTI
               COID

=> d his


     (FILE 'HOME' ENTERED AT 13:27:17 ON 30 SEP 1999)

     FILE 'REGISTRY' ENTERED AT 13:27:24 ON 30 SEP 1999
                E MIFEPRISTONE/CN
L1            1 S E3
                E RU009/CN
                E RU 009/CN
                E RU 9/CN
                E RU 39.009/CN
L2            1 S E5
                E RU 044/CN
                E RU 43044/CN
L3            1 S E3
                E RU 44/CN
L4            1 S E3

     FILE 'CA, BIOSIS, MEDLINE, DRUGU, EMBASE' ENTERED AT 13:34:40 ON 30 SEP
     1999
L5        11834 S L1 OR L2 OR L3 OR L4 OR RU486 OR RU 486 OR MIFEPRISTONE OR
RU
L6       463846 S PSYCHOSIS OR PSYCHOT? OR ANTIPSYCHO? OR SCHIZO? OR ALZHEIM?
O
L7           50 S L5 AND L6
L8           36 DUP REM L7 (14 DUPLICATES REMOVED)
L9        17076 S (GLUCOCORTICOID? OR CORTISOL OR
HYDROCORTISONE)(2A)(ANTAGONIS

=> s dilus? or hallucinat?

L10      19134 DILUS? OR HALLUCINAT?

=> s l9 and (l6 or l10)

L11        109 L9 AND (L6 OR L10)

=> s l11 not l7

L12         94 L11 NOT L7

=> dup rem l12

PROCESSING COMPLETED FOR L12
L13          58 DUP REM L12 (36 DUPLICATES REMOVED)
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=> d 1-58 bib,ab

L13 ANSWER 1 OF 58 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1999-22986 DRUGU P
TI Interrelationship between substrates and inhibitors of human CYP3A and p-glycoprotein.
AU Kim R B; Wandel C; Leake B; Cvetkovic M; Fromm M F; Dempsey P J; Roden M M; Belas F; Chaudhary A K; Roden D M; Wood A J J; Wilkinson G R
CS Univ.Vanderbilt
LO Nashville, Tenn., USA
SO Pharm.Res. (16, No. 3, 408-14, 1999) 4 Fig. 2 Tab. 29 Ref.
CODEN: PHREEB ISSN: 0724-8741
AV Departments of Medicine and Pharmacology, Vanderbilt University, School of Medicine, Nashville, Tennessee 37232-6602, U.S.A. (e-mail: richard.kim@mcmail.vanderbilt.edu).
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB The aim of these studies were to determine the p-glycoprotein (P-gp)-mediated transport and inhibitory characteristics of prototypical CYP substrates; terfenadine, quinidine, PSC-833, ketoconazole, verapamil, amiodarone, lovastatin, erythromycin, midazolam, tamoxifen, nifedipine, 1-hydroxymidazolam, 6-beta-hydroxycortisol, cortisol, caffeine, tolbutamide, S-mephenytoin, debrisoquine and chlorzoxazone in vitro and mice. Some CYP3A substrates terfenadine, erythromycin and lovastatin but not nifedipine or midazolam were found to be P-gp substrates. None of the prototypical substrates of other common human CYP isoforms were transported by P-gp with the exception of debrisoquine. These data demonstrate the overlap in substrate specificities of CYP3A and P-gp appears to be by chance rather than being indicative of a significant relationship.

L13 ANSWER 2 OF 58 CA COPYRIGHT 1999 ACS DUPLICATE 1
AN 130:148567 CA
TI Neuroactive steroid concentrations following metyrapone administration in depressed patients and healthy volunteers
AU Rupprecht, Rainer; Strohle, Andreas; Hermann, Bettina; Michele, Flavia di; Spalletta, Gianfranco; Pasini, Augusto; Holsboer, Florian; Romeo, Elena
CS Max Planck Institute of Psychiatry, Clinical Institute, Munich, Germany
SO Biol. Psychiatry (1998), 44(9), 912-914
CODEN: BIPCBF; ISSN: 0006-3223
PB Elsevier Science Inc.
DT Journal
LA English
AB Background: There is evidence that treatment with the 11.beta.-hydroxylase inhibitor metyrapone may represent an alternative treatment strategy in major depression. As a consequence of **inhibition** of **cortisol** synthesis the overdrive of corticotropin leads to an accumulation of precursor steroids. However, the effects of metyrapone on the concns. of endogenous neuroactive steroids that modulate ion channels, e.g., the GABAA receptor, have not yet been studied systematically. Methods: Therefore, we quantified the concns. of an array of neuroactive steroids following administration of 1.5g metyrapone before and after pretreatment with 1 mg dexamethasone in 19 patients suffering from severe depression in comparison to 13 healthy controls by means of a highly sensitive gas chromatog./mass spectrometry anal. Results: The

administration of metyrapone induced a pronounced increase in all neuroactive steroids studied both in patients and controls that was prevented by dexamethasone pretreatment. Conclusions: Thus, the **psychotropic** properties of endogenous neuroactive steroids may contribute to the antidepressant properties of metyrapone in the treatment of major depression.

L13 ANSWER 3 OF 58 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1998-42500 DRUGU P
TI Effect of theophylline, caffeine and dimethylxanthines on endogenous glucocorticoid levels in mice. A possible mechanism of anti-inflammatory activity of theophylline.
AU Sato J; Hori S; Kawamura M
CS Univ.Jikei
LO Tokyo, Jap.
SO Pharm.Pharmacol.Commun. (4, No. 10, 499-501, 1998) 1 Fig. 2 Tab. 10 Ref. ISSN: 1460-8081
AV Department of Pharmacology, Jikei University School of Medicine, 3-25-8 Nishi-Shinbashi, Minato-ku, Tokyo 105-8461, Japan. (S.H.).
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB The effects of theophylline, caffeine and dimethylxanthines on endogenous glucocorticoid levels were determined in mice. I.p. theophylline increased serum glucocorticoid levels in a dose-dependent manner.Whilst pentoxifylline, theobromine and xanthine did not affect serum glucocorticoid levels, caffeine, 1,7-dimethylxanthine and aminophylline (all i.p.) were associated with increases in serum glucocorticoid. Pre-treatment with dexamethasone completely **inhibited** **glucocorticoidogenesis** induced by theophylline. Theophylline, a bronchodilator used in obstructive airway diseases, shows anti-inflammatory activity, modulates IL production in mononuclear cells and regulates active oxygen production in both neutrophils and mononuclear cells. Glucocorticoid shows strong anti-inflammatory activity.

L13 ANSWER 4 OF 58 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1999-06187 DRUGU P E
TI Antidepressants **inhibit** the **glucocorticoid** stimulation of thyrotropin releasing hormone expression in cultured hypothalamic neurons.
AU Jackson I M D; Luo L G
CS Univ.Brown
LO Providence, R.I., USA
SO J.Invest.Med. (46, No. 9, 470-74, 1998) 3 Fig. 23 Ref. ISSN: 1081-5589
AV Division of Endocrinology, Rhode Island Hospital, 593 Eddy Street, Providence, RI 02903, U.S.A.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB The effect of the antidepressants imipramine (IM, Sigma-Chem.), desipramine HCl (DE, Sigma-Chem.), sertraline (SE, Sigma-Chem.), and fluoxetine (FL, Lilly) on thyroliberin (TRH) secretion was investigated in a fetal rat hypothalamic neuronal culture system. The antidepressants did not affect cellular morphology, but inhibited both basal and glucocorticoid (dexamethasone) stimulation of TRH secretion. The results suggest that the effect of antidepressants (of the tricyclic and SSRI

variety) on the thyroid axis in depression might result in part from a direct non-toxic action on the TRH neuron. Studies have shown that thyroid function regresses to normal when antidepressants are clinically efficacious. Other mechanisms may need to be invoked in addition, however, since basal TRH content was also reduced.

L13 ANSWER 5 OF 58 MEDLINE
AN 1998181525 MEDLINE
DN 98181525
TI Increased total 7 alpha-hydroxy-dehydroepiandrosterone in serum of patients with **Alzheimer**'s disease.
AU Attal-Khemis S; Dalmeyda V; Michot J L; Roudier M; Morfin R
CS Conservatoire National des Arts et Metiers, Paris, France.
SO JOURNALS OF GERONTOLOGY. SERIES A, BIOLOGICAL SCIENCES AND MEDICAL SCIENCES, (1998 Mar) 53 (2) B125-32.
Journal code: CBA. ISSN: 1079-5006.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199806
EW 19980603
AB Evidence has indicated that circulating adrenal steroid quantitites were significantly changed in patients with **Alzheimer**'s disease (AD). Aside of 3 beta-sulfatation and 3 beta-acylations, levels of dehydroepiandrosterone (DHEA) result from production and metabolic transformation yields. 7 alpha-Hydroxylation of DHEA has been described in humans, and 7 alpha-hydroxy-DHEA may be responsible for the known **antiglucocorticoid** effects of DHEA. Using a negative ion fragmentometry method with gas chromatography/mass spectrometry on trifluoroacetate derivatives, we measured levels of free 7 alpha-hydroxy-DHEA as well as its sulfated conjugate and its fatty acid esters in serum of 10 female patients with AD and of 8 age-matched healthy control women. Free 7 alpha-hydroxy-DHEA levels in AD and controls were not significantly different (240.2 +/- 37.2 pg/ml and 206.8 +/- 21.6 pg/ml, respectively), but sulfate conjugate levels were significantly increased in AD (p = .01) (262 +/- 28.4 and 145.4 +/- 27.6, respectively) as well as fatty acid esters (p = .041) (65.7 +/- 6.9 and 40.7 +/- 9.2, respectively). These results indicated that the total 7 alpha-hydroxy-DHEA produced was significantly increased in AD (p = .024) and may contribute to the disease-related disturbances of DHEA production and metabolism.

L13 ANSWER 6 OF 58 BIOSIS COPYRIGHT 1999 BIOSIS DUPLICATE 2
AN 1998:324841 BIOSIS
DN PREV199800324841
TI Treatment-resistant depression: Clinical significance, concept and management.
AU Sharan, P. (1); Saxena, S.
CS (1) Dep. Psychiatry, Postgrad. Inst. Med. Educ. Res., Chandigarh 160 012 India
SO National Medical Journal of India, (March-April, 1998) Vol. 11, No. 2, pp. 69-79.
ISSN: 0970-258X.
DT General Review
LA English
AB Depression is a common disorder which causes intense personal suffering and socio-occupational dysfunction. It also imposes a heavy economic burden on society. It has been shown that between 29% and 46% of depressed patents fall to respond adequately to antidepressant medication. Treatment-resistant depression may contribute to the morbidity and

mortality associated with affective illness. When treatment resistance is suspected, the patents history should be reevaluated particularly regarding diagnostic subtypes and comorbidity. An assessment of treatment adequacy in terms of dose, duration and compliance should also be made. Treatment strategies for treatment-resistant depression should be systematic and empirically grounded because of the risk of increased resistance and loss of time in case of a random trialand-error approach, and the inherent risks in certain novel strategies. A stepped care approach to treatment-resistant depression involves optimization of the current drug under trial, augmentation with drugs such as lithium and triiodothyronine, and switching to other somatic therapies such as electroconvulsive therapy and monoamine inhibitors. Only if these strategies fail, should novel treatments such as the use of venlafaxine, antidepressant combinations and augmentation with sleep deprivation be considered. Experimental strategies such as the use of **antiglucocorticoids** and sex hormones, which carry considerable risk, should be restricted to research settings. Somatotherapy should be combined in all cases with depression-specific **psychotherapy**. Psychosurgery should be considered only in truly intractable cases. Rational and energetic treatment can adequately help a large majority of patients with treatment-resistant depression.

L13 ANSWER 7 OF 58 CA COPYRIGHT 1999 ACS DUPLICATE 3
AN 130:291103 CA
TI Ketoconazole reduces low dose cocaine self-administration in rats
AU Goeders, Nick E.; Peltier, Rachel L.; Guerin, Glenn F.
CS Department of Pharmacology and Therapeutics, Louisiana State University Medical Center, Shreveport, LA, 71130-3932, USA
SO Drug Alcohol Depend. (1998), 53(1), 67-77
CODEN: DADEDV; ISSN: 0376-8716
PB Elsevier Science Ireland Ltd.
DT Journal
LA English
AB Ketoconazole is an oral antimycotic agent approved by the FDA for the treatment of fungal disease which also blocks the synthesis of adrenocorticosteroids and functions as a **glucocorticoid** receptor **antagonist**. In these expts., adult male Wistar rats were allowed alternating 15-min periods of access to food reinforcement and cocaine self-administration (0.125, 0.25 or 0.5 mg/kg per infusion) during daily 2-h sessions. A 1-min timeout sepd. access to the two reinforcers. Pretreatment with ketoconazole (25 mg/kg, i.p.) significantly decreased plasma corticosterone and reduced low dose (i.e. 0.125-0.25 mg/kg per infusion) cocaine self-administration without affecting food-reinforced responding. In fact, pretreatment with ketoconazole resulted in rates and patterns of self-administration at these doses that were indistinguishable from those obsd. during cocaine extinction. However, cocaine self-administration at the highest dose tested in these expts. (i.e. 0.5 mg/kg per infusion) was not significantly affected by ketoconazole. These data suggest the potential utility of ketoconazole or related drugs as adjuncts in the treatment of **cocaine abuse** and further underscore the role for corticosterone in cocaine reinforcement.

L13 ANSWER 8 OF 58 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1998-14294 DRUGU P E
TI A comparison of the effects of metyrapone with the tricyclic antidepressant desipramine in the forced swim antidepressant test.
AU Healy D G; Kelly J P; Leonard B E
CS Univ.Coll.Galway
LO Galway, Ire.
SO Ir.J.Med.Sci. (167, No. 1, 60, 1998) 1 Tab. 2 Ref.
CODEN: IJMSAT ISSN: 0021-1265

AV Department of Pharmacology, University College, Galway, Ireland.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB A possible antidepressant action of the **glucocorticoid** synthesis **inhibitor**, i.p. metyrapone, was investigated in comparison with i.p. desipramine (DMI), in the forced swimming test (FST) in rats. Both MP and DMI reduced the immobility time, but s.c. corticosterone (CS) was only able to reverse the effects of MP. Thus, the efficacy of MP in the FST is hypothalamo-pituitary-adrenal cortical axis-dependent whereas DMI's is CS-independent, suggestive of different mechanisms of action in this paradigm. (conference abstract).

L13 ANSWER 9 OF 58 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 1998098858 EMBASE
TI Increased total 7.alpha.-hydroxy-dehydroepiandrosterone in serum of patients with **Alzheimer**'s disease.
AU Attal-Khemis S.; Dalmeyda V.; Michot J.-L.; Roudier M.; Morfin R.
CS Prof. R. Morfin, Biologie, CNAM, 2 rue Conte, 75003 Paris, France
SO Journals of Gerontology - Series A Biological Sciences and Medical Sciences, (1998) 53/2 (B125-B132).
Refs: 60
ISSN: 1079-5006 CODEN: JGASFW
CY United States
DT Journal; Article
FS 005 General Pathology and Pathological Anatomy
020 Gerontology and Geriatrics
LA English
SL English
AB Evidence has indicated that circulating adrenal steroid quantitites were significantly changed in patients with **Alzheimer**'s disease (AD). Aside of 3.beta.-sulfatation and 3.beta.-acylations, levels of dehydrospiandrosterone (DHEA) result from production and metabolic transformation yields. 7.alpha.-Hydroxylation of DHEA has been described in humans, and 7.alpha.-hydroxy-DHEA may be responsible for the known **antiglucocorticoid** effects of DHEA. Using a negative ion fragmentometry method with gas chromatography/mass spectrometry on trifluoroacetate derivatives, we measured levels of free 7.alpha.-hydroxy-DHEA as well as its sulfated conjugate and its fatty acid esters in serum of 10 female patients with AD and of 8 age-matched healthy control women. Free 7.alpha.- hydroxy-DHEA levels in AD and controls were not significantly different (240.2 .+-. 37.2 pg/ml and 206.8 .+-. 21.6 pg/ml, respectively), but sulfate conjugate levels were significantly increased in AD (p = .01) (262 .+-. 28.4 and 145.4 .+-. 27.6, respectively) as well as fatty acid esters (p = .041) (65.7 .+-. 6.9 and 40.7 .+-. 9.2, respectively). These results indicated that the total 7.alpha.-hydroxy-DHEA produced was significantly increased in AD (p = .024) and may contribute to the disease-related disturbances of DHEA production and metabolism.

L13 ANSWER 10 OF 58 MEDLINE DUPLICATE 4
AN 97305509 MEDLINE
DN 97305509
TI The relationship of endogenous cortisol to psychiatric disorder: a review.
AU Kiraly S J; Ancill R J; Dimitrova G
CS St Vincent's Hospital, Vancouver, British Columbia.
SO CANADIAN JOURNAL OF PSYCHIATRY. REVUE CANADIENNE DE PSYCHIATRIE, (1997 May) 42 (4) 415-20. Ref: 85
Journal code: CLR. ISSN: 0706-7437.
CY Canada

DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199710
AB OBJECTIVES: To focus on hypothalamic-pituitary-adrenal (HPA) axis activity, especially endogenous hypercortisolemia, to study its role in the maintenance of psychiatric illness, and to entertain the probability that the elderly are vulnerable. METHOD: Case presentation, clinical and research literature review, and theoretical discussion. RESULTS: Clinical and research evidence overwhelmingly suggest that hypercortisolemia is toxic to the hippocampus. Some research supports the position that it can be a treatable perpetuating factor in a subset of affective disorders and psychoses. Pharmacological treatments to correct hypercortisolemia have been used by endocrinologists. Hypercortisolemic treatment-resistant and nontreatment-resistant psychoses and affective disorders have been successfully treated by a small number of researchers who remain interested in this subject. Data pertaining to geriatric psychoses may be germane but are sparse. CONCLUSIONS: It behooves us to research diagnostic methods pertaining to psychoses and affective disorders associated with hypercortisolemic states. Very little research is available, but we must be alert to the possibility that the elderly are more susceptible to cortisol endotoxicosis than the younger adult population. Without accurate diagnosis, we cannot take advantage of existing **antiglucocorticoid** strategies.

L13 ANSWER 11 OF 58 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 97185194 EMBASE
DN 1997185194
TI [Progress in psychoendocrinology of sexual- and stresshormones].
UJ ADATOK A SZEXUAL- ES STRESSZHORMONOK PSZICHOENDOKRINOLOGIAJAHOZ.
AU Molnar G.
CS Dr. G. Molnar, Levelcim, Csapo u. 61. 3/5, 4029 Debrecen, Hungary
SO Gyogyszereszet, (1997) 41/4 (225-229).
Refs: 33
ISSN: 0017-6036 CODEN: GYOGAI
CY Hungary
DT Journal; General Review
FS 003 Endocrinology
008 Neurology and Neurosurgery
010 Obstetrics and Gynecology
032 Psychiatry
030 Pharmacology
037 Drug Literature Index
LA Hungarian
SL Hungarian; English
AB Manfred Bleuler summarized the concept of endocrine psychosyndrome in 1959, which was an aspecific, restricted disturbance of emotional life and instinct behaviour associated with hormonal diseases. In the past 35 years, psychoendocrinology made a valuable contribution to psychiatry. Since 1990, a lot of experiences have been accumulated on the high therapeutical response rate of selective serotonin reuptake inhibitors in premenstrual syndrome (late luteal phase dysphoric disorder). Positive correlations were found between the severities of depressions and FSH serum levels in postmenopausal major depressions. Increased FSH-release might be an indicator of diminished estrogen effect in this mental disorder. The lowest estradiol serum levels were found in demented female patients. Estrogen and DHEA (precursor of estradiol and testosterone) treatments had contraversial therapeutical results in **Alzheimer**'s dementias. Regarding Sulser's serotonin (norepinephrine) glucocorticoid

link hypothesis, high cortisol level in major depression could exert influence on neurotransmitter cell-effects inducing secondary depressiogenic biochemical changes. **Antiglucocorticoids** with antidepressive properties presented the new approach in the treatment of depression. Research on high CRH-release in major depression had very many to accept the direct pathogenetic contribution of CRH-effect to the development of major depression. Discovery of neurosteroids being synthetized in the brain opened new directions in the **psychotropic** drug development. Research of the 1990-ies began to form the molecular biological bases of endocrine-neurotransmitrer interactions.

L13 ANSWER 12 OF 58 CA COPYRIGHT 1999 ACS DUPLICATE 5
AN 128:136418 CA
TI NSAIDS inhibit the IL-1.beta.-induced IL-6 release from human post-mortem astrocytes: the involvement of prostaglandin E2
AU Blom, Michaela A. A.; van Twillert, Margriete G. H.; de Vries, Sabine C.; Engels, F.; Finch, Caleb E.; Veerhuis, Robert; Eikelenboom, Piet
CS Department of Psychiatry, Research Institute Neurosciences Vrije Universiteit, Graduate School Neurosciences Amsterdam, Academic Hospital Vrije Universiteit Amsterdam, Amsterdam, Neth.
SO Brain Res. (1997), 777(1,2), 210-218
CODEN: BRREAP; ISSN: 0006-8993
PB Elsevier Science B.V.
DT Journal
LA English
AB Epidemiol. studies have shown that steroidal as well as non-steroidal anti-inflammatory drugs lower the risk of developing **Alzheimer**'s Disease (AD). A suppressive effect of these anti-inflammatory drugs on local inflammatory events in AD brains has been suggested, however the mechanisms responsible are still unknown. In this study we investigated at cellular level the influence of two anti-inflammatory drugs - dexamethasone and indomethacin - and an exptl. specific cyclooxygenase-2 inhibitor, BF389, on the prodn. of the pro-inflammatory cytokine IL-6 and the inflammatory mediator PGE2 by human astrocytes. Two human post-mortem astrocyte cultures (A157 and A295) and astroglioma cell lines (U251 and U373 MG) were found to secrete considerable amts. of IL-6 upon stimulation with IL-1.beta.. The **glucocorticoid** dexamethasone **inhibited** the IL-1.beta.-activated release of IL-6 from the postmortem astrocyte cultures A157 and A295 and from the astroglioma cell lines. The non-specific cyclooxygenase inhibitor indomethacin and BF389 only suppressed the IL-6 release by post-mortem astrocyte culture A157. This post-mortem astrocyte culture was found to produce large amts. of PGE2 upon stimulation with IL-1.beta., whereas in the supernatants of the postmortem astrocyte culture A295 and the astroglioma cell lines, low PGE2 concns. were detected. Addn. of exogenous PGE2 prevented the inhibitory effect of indomethacin and BF389 on the IL-1.beta.-activated IL-6 release from A157 astrocytes and largely potentiated the IL-1-induced release of IL-6 from all astrocytes/astroglioma cells tested. Dexamethasone also inhibited the PGE2 release from the astrocytes and astroglioma cells, however the inhibitory effect of dexamethasone on the IL-1.beta.-activated IL-6 release could not be prevented by the addn. of PGE2. The obsd. redn. of IL-6 and/or PGE2 from astrocytes may be involved in the mechanism underlying the beneficial effects of these drugs in AD.

L13 ANSWER 13 OF 58 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1997:405462 BIOSIS
DN PREV199799711665
TI **Antiglucocorticoid** treatments in psychiatry.
AU Reus, Victor I. (1); Wolkowitz, Owen M.; Frederick, Sydney

CS (1) 401 Parnassus Ave., Bos F-0984, San Francisco, CA 94143-0984 USA
SO Psychoneuroendocrinology, (1997) Vol. 22, No. SUPPL. 1, pp. S121-S124. ISSN: 0306-4530.
DT General Review
LA English
AB A confluence of evidence indicates that alterations in hypothalamic-pituitary-adrenal regulation can have profound effects on the symptom picture of psychiatric illnesses and that therapeutic interventions directly targeted at corticosteroid metabolism may have clinical benefit. This paper reviews the varying lines of inference that support such a hypothesis and reviews work by our group and others utilizing the **cortisol** synthesis **inhibitor**, ketoconazole and, more recently, dehydroepiandrosterone (DHEA), as potential novel mood-altering agents. The data thus far suggest that **antiglucocorticoid** drug treatment may be useful in certain subgroups of depressed patients and may offer a theoretical rationale for alternative drug design.

L13 ANSWER 14 OF 58 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1997-25546 DRUGU P E
TI Blunted nocturnal cortisol release after GHRH in male, but not in female patients with depression.
AU Steiger A; Antonijevic I A; Frieboes R M; Murck H
CS Max-Planck-Inst.Psychiat.
LO Munich, Ger.
SO Exp.Clin.Endocrinol.Diabetes (105, Suppl. 1, 33, 1997) 1 Ref.
ISSN: 0947-7349
AV Max Planck Institute of Psychiatry, Clinical Institute, Department of Psychiatry, Munich, Germany.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB Sex differences in the nocturnal cortisol secretory response to i.v. somatoliberin (GHRH) were investigated in 32 patients with major depression, enrolled in a randomized, placebo (PL)-controlled study. There were no significant effects on sleep EEG and on ACTH levels in both sexes. However, the data suggested acute antagonistic properties of GHRH on cortisol secretion, which is frequently elevated during depression, in male, but not in female depressed patients. (conference abstract).

L13 ANSWER 15 OF 58 MEDLINE
AN 96301625 MEDLINE
DN 96301625
TI Geriatric endogenous cortisol **psychosis**--role of **cortisol antagonists** [letter].
AU Kiraly S J; Ancill R J
SO CANADIAN JOURNAL OF PSYCHIATRY. REVUE CANADIENNE DE PSYCHIATRIE, (1996 Apr) 41 (3) 193.
Journal code: CLR. ISSN: 0706-7437.
CY Canada
DT Letter
LA English
FS Priority Journals
EM 199701

L13 ANSWER 16 OF 58 CA COPYRIGHT 1999 ACS DUPLICATE 6
AN 126:84476 CA
TI Suppression of glucocorticoid secretion and **antipsychotic** drugs have similar effects on the mesolimbic dopaminergic transmission
AU Piazza, Pier Vincenzo; Barrot, Michel; Rouge-Pont, Francoise; Marinelli,

Michela; Maccari, Stefania; Abrous, Djoher; Simon, Herve; Le Moal, Michel
CS Lab. Psychobiol. Comportements Adaptatifs, Univ. Bordeaux II, Bordeaux, 33077, Fr.
SO Proc. Natl. Acad. Sci. U. S. A. (1996), 93(26), 15445-15450
CODEN: PNASA6; ISSN: 0027-8424
PB National Academy of Sciences
DT Journal
LA English
AB Specific antagonists of central dopaminergic receptors constitute the major class of **antipsychotic** drugs (APD). Two principal effects of APD are used as criteria for the pre-clin. screening of their **antipsychotic** action: (i) inhibition of basal and depolarization-induced activity of mesolimbic dopaminergic neurons; (ii) antagonism of the locomotor effects of dopaminergic agonists. Given that glucocorticoid hormones in animals increase dopamine release and dopamine-mediated behaviors and that high levels of glucocorticoids can induce **psychotic** symptoms in humans, these expts. examd. whether **inhibition** of endogenous **glucocorticoids** might have APD-like effects on mesolimbic dopaminergic transmission in rats. It is shown that suppression of glucocorticoid secretion by adrenalectomy profoundly decreased (by greater than 50%): (i) basal dopaminergic release and the release of dopamine induced by a depolarizing stimulus such as morphine (2 mg/kg, s.c.), as measured in the nucleus accumbens of freely moving animals by microdialysis; (ii) the locomotor activity induced by the direct dopaminergic agonist apomorphine. The effects of adrenalectomy were glucocorticoid specific given that they were reversed by the administration of glucocorticoids at doses within the physiol. range. Despite its profound diminution of dopaminergic neurotransmission, adrenalectomy neither modified the no. of mesencephalic dopaminergic neurons nor induced gliosis in the mesencephalon or in the nucleus accumbens, as shown by tyrosine hydroxylase and glial fibrillary acidic protein immunostaining. In conclusion, these findings suggest that blockade of central effects of glucocorticoids might open new therapeutic strategies of behavioral disturbances.

L13 ANSWER 17 OF 58 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 96204960 EMBASE
DN 1996204960
TI Metyrapone, an **inhibitor** of **glucocorticoid** production, reduces brain injury induced by focal and global ischemia and seizures.
AU Smith-Swintosky V.L.; Pettigrew L.C.; Sapolsky R.M.; Phares C.; Craddock S.D.; Brooke S.M.; Mattson M.P.
CS 211 Sanders-Brown Building, University of Kentucky,Lexington, KY 40536-0230, United States
SO Journal of Cerebral Blood Flow and Metabolism, (1996) 16/4 (585-598).
ISSN: 0271-678X CODEN: JCBMDN
CY United States
DT Journal; Article
FS 008 Neurology and Neurosurgery
LA English
SL English
AB Increasing evidence indicates that glucocorticoids (GCs), produced in response to physical/emotional stressors, can exacerbate brain damage resulting from cerebral ischemia and severe seizure activity. However, much of the supporting evidence has come from studies employing nonphysiological paradigms in which adrenalectomized rats were compared with those exposed to constant GC concentrations in the upper physiological range. Cerebral ischemia and seizures can induce considerable GC secretion. We now present data from experiments using metyrapone (an 11-.beta.-hydroxylase inhibitor of GC production), which demonstrate that the GC stress-response worsens subsequent brain damage induced by ischemia and seizures in rats. Three different paradigms of brain injury were employed: middle cerebral artery occlusion (MCAO) model

of focal cerebral ischemia; four-vessel occlusion (4VO) model of transient global forebrain ischemia; and kainic acid (KA)-induced (seizure-mediated) excitotoxic damage to hippocampal CA3 and CA1 neurons. Metyrapone (200 mg/kg body wt) was administered systemically in a single i.p. bolus 30 min prior to each insult. In the MCAO model, metyrapone treatment significantly reduced infarct volume and also preserved cells within the infarct. In the 4VO model, neuronal loss in region CA1 of the hippocampus was significantly reduced in rats administered metyrapone. Seizure-induced damage to hippocampal pyramidal neurons (assessed by cell counts and immunochemical analyses of cytoskeletal alterations) was significantly reduced in rats administered metyrapone. Measurement of plasma levels of corticosterone (the species-typical GC of rats) after each insult showed that metyrapone significantly suppressed the injury-induced rise in levels of circulating corticosterone. These findings indicate that endogenous corticosterone contributes to the basal level of brain injury resulting from cerebral ischemia and excitotoxic seizure activity and suggest that drugs that suppress glucocorticoid production may be effective in reducing brain damage in stroke and epilepsy patients.

L13 ANSWER 18 OF 58 MEDLINE DUPLICATE 7
AN 96424727 MEDLINE
DN 96424727
TI Management of **psychotic**, treatment-resistant depression.
AU Rothschild A J
CS Department of Psychiatry, Harvard Medical School, Boston, Massachusetts, USA.
NC MH-47457 (NIMH)
SO PSYCHIATRIC CLINICS OF NORTH AMERICA, (1996 Jun) 19 (2) 237-52. Ref: 119
Journal code: PBN. ISSN: 0193-953X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199612
AB As there are no controlled studies on approaches to patients with treatment-resistant **psychotic** depression many questions remain to be answered. Those that seem worthy of high priority include (1) the efficacy of novel **antipsychotic** agents (e.g., clozapine, risperidone) for acute and maintenance treatment; (2) the efficacy of newer antidepressant agents such as the SSRIs and nefazodone plus neuroleptic medications; (3) decision trees to delineate the second and third lines of treatment when the first treatment is ineffective; (4) the comparative efficacy of bilateral versus unilateral ECT; (5) the length of time patients should be maintained on medications (which is of particular importance in the case of neuroleptic agents with their potential to cause tardive dyskinesia); (6) the optimal dose of neuroleptic agent for acute treatment; (7) the optimal length of time for medication trials; (8) the use of antidepressant medications during ECT treatments; (9) the importance of the sequence in which TCAs and neuroleptic agents are administered; (10) the delineation of the clinical characteristics of responders to medication versus ECT treatments; and (11) the role of **antiglucocorticoid** strategies. The answers to these questions would provide clinicians with important tools to treat patients with **psychotic** depression, an illness that all too frequently can become treatment-resistant.

L13 ANSWER 19 OF 58 BIOSIS COPYRIGHT 1999 BIOSIS DUPLICATE 8
AN 1996:467928 BIOSIS
DN PREV199699190284

TI Trimipramine: A challenge to current concepts on antidepressives.
AU Berger, M. (1); Gastpar, M.
CS (1) Klinikum der Albert-Ludwigs-Univ., Universitatsklinik fur Psychiatrie und Psychosomatik, Hauptstrasse 5, D-79104 Freiburg Germany
SO European Archives of Psychiatry and Clinical Neuroscience, (1996) Vol. 246, No. 5, pp. 235-239.
ISSN: 0940-1334.
DT Article
LA English
AB Although it is chemically a classical tricyclic antidepressant agent, trimipramine shows atypical pharmacological properties. Its well-documented antidepressant action cannot be explained by noradrenaline or serotonin reuptake inhibition or by a down-regulation of beta-adrenoceptors. Furthermore, its receptor affinity profile resembles more that of clozapine, a neuroleptic drug, than that of tricyclic antidepressants. Trimipramine does not reduce, but rather increases, rapid eye movement sleep. It stimulates nocturnal prolactin secretion and **inhibits** nocturnal **cortisol** secretion, and may act at the level of the hypothalamus on corticotropin-releasing hormone secretion. Trimipramine is of particular value in depressed patients with insomnia, and it has been shown to be effective in the therapy of primary insomnia. As the pharmacological profile indicates, and an open clinical study has shown, trimipramine might also be active as an **antipsychotic**. The drug is both a tool for increasing our understanding of depression and a potential therapy for several psychiatric disorders.

L13 ANSWER 20 OF 58 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 96344775 EMBASE
DN 1996344775
TI [Endocrinology and **Alzheimer**'s disease].
ENDOKRINOLOGIE UND MORBUS **ALZHEIMER**.
AU Eber O.
CS Bergstrasse 27,A-8020 Graz, Austria
SO Neuropsychiatrie, (1996) 10/3 (128-133).
ISSN: 0948-6259 CODEN: NUROF
CY Germany
DT Journal; (Short Survey)
FS 003 Endocrinology
032 Psychiatry
LA German
SL German; English
AB New concepts in the rapidly expanding field of endocrinology must be elucidated to benefit from the extensive research of the neuro-immuno-endocrine network. In order to place these advances in a proper perspective it is necessary to widen the scope of classical endocrinology. In **Alzheimer**'s disease (AD) the main changes in the endocrine system result from a longstanding activation of the HPA-axis due to permanent stress. The final effect of this prolonged hypercortisolism is a neurotoxic damage to the hippocampus which is the key regulator of the HPA system. The task of the hippocampus within the neuroendocrinological network is to stop exaggerating stress response. However, persistent downregulations of the corticoid receptors in the hippocampus will disrupt the negative feedback and lead to further increase in corticosteroids ('glucocorticoid cascade hypothesis'). On the other hand the hippocampus is an important region of memory storage and processing, deficits of which represent key features of AD; thus, a serious hippocampal neuronal loss, qualitatively different to normal aging, is one of the main features of AD. DHEA represents the androgen hormone of the adrenal cortex and its gradual decrease covering the entire span of life has generally been accepted in normal human aging whith

cortisol levels remaining unchanged. However, in AD this decrease in DHEA serum and CSF concentrations is far more pronounced; thus, the potent **antiglucocorticoid** effects of DHEA is vanishing. It must be stated that DHEA is not only produced peripherally but also within the CNS and additionally, in the brain there are specific receptors for this 'neurosteroid'. Clinically the DHEA/cortisol ratio may be used as a marker in those AD-patients who are prone to neurotoxic glucocorticoid effects. Thyroid diseases have been observed prior to AD significantly more frequently than in controls. Patients with Down's syndrome, a condition often associated with hypothyroidism or thyroid autoantibodies, inevitably end up with AD. The genetic location of Down's syndrome, familial AD. and amyloid precursor protein, are closely adjoining along chromosome 21. In treatment of AD the cholinergic effect of high doses of TRH was utilized for a number of years. Transthyretin the main thyroxine transport protein in CSF was supposed to be associated with amyloid formation.

L13 ANSWER 21 OF 58 CA COPYRIGHT 1999 ACS DUPLICATE 9
AN 122:205106 CA
TI Effects of neuroleptic treatment on cortisol and 3-methoxy-4-hydroxyphenylethyl glycol levels in blood
AU Wik, G.
CS Dep. Clinical Neuroscience, Karolinska Hosp., Stockholm, S-171 76, Swed.
SO J. Endocrinol. (1995), 144(3), 425-29
CODEN: JOENAK; ISSN: 0022-0795
DT Journal
LA English
AB Plasma cortisol and serum 3-methoxy-4-hydroxyphenylethyl glycol (MHPG) were detd. before and after 5-6 wk of neuroleptic treatment in patients with **schizophrenia**. Following drug treatment both plasma cortisol and serum MHPG levels in patients decreased and plasma cortisol levels were also lower than in unmedicated healthy controls. Indications of a relation between the redn. of cortisol and MHPG levels were found. The data show that neuroleptic drug treatment **inhibits cortisol** secretion. It is speculated that this inhibition could be related to reduced noradrenergic activity.

L13 ANSWER 22 OF 58 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1995:211267 BIOSIS
DN PREV199598225567
TI The **psychotropic** effects of inhibitors of steroid biosynthesis in depressed patients refractory to treatment.
AU Ghadirian, A. Missagh (1); Engelsmann, Frank; Dhar, Veena; Filipini, Daniel; Keller, Robert; Chouinard, Guy; Murphy, Beverly E. Pearson
CS (1) Allan Memorial Inst., 1025 Pine Ave. West, Montreal H41 1A1 Canada
SO Biological Psychiatry, (1995) Vol. 37, No. 6, pp. 369-375.
ISSN: 0006-3223.
DT Article
LA English
AB Twenty patients, diagnosed as suffering from treatment-resistant major depression, were treated with one or more drugs that decrease corticosteroid biosynthesis. Nine were **psychotic**, 11 nonpsychotic. Seventeen completed the treatment (8 **psychotic**, 9 nonpsychotic); 13 responded (5 **psychotic**, 8 nonpsychotic); 11 responded completely (i.e., a drop in the Hamilton Depression Scale of at least 50%, to ltoreq 15), and 2 responded partially. The mean age of the responders (45.2 +- 12.6 years) did not differ significantly from that of the nonresponders (48.7 +- 12/13). Data were analyzed in the following categories; (1) the presence or absence of **psychosis**, (2) response or nonresponse to treatment, and (3) the drug(s) used (aminoglutethimide, ketoconazole, or a combination of either of these with metyrapone). The patients improved over time on the Hamilton Depression Scale independent of the medication used. Responders demonstrated

improvement in mood, insomnia, anxiety, diurnal variation, paranoia and obsessive compulsiveness. Nonpsychotics responded better than **psychotics**.

L13 ANSWER 23 OF 58 CA COPYRIGHT 1999 ACS
AN 122:72050 CA
TI Apoptosis inhibitors for treating neurodegenerative diseases
IN Rubin, Lee Laurence; Brooks, Susan Frances
PA Eisai Co., Ltd., Japan
SO PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9427583	A2	19941208	WO 1994-GB1169	19940531
	WO 9427583	A3	19950202		
	W: JP, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 700286	A1	19960313	EP 1994-916326	19940531
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 09504780	T2	19970513	JP 1994-500413	19940531
	US 5840719	A	19981124	US 1996-556974	19960508
PRAI	GB 1993-11132		19930528		
	WO 1994-GB1169		19940531		

AB Apoptotic cell death in a fully differentiated, non-dividing cell such as neuron is caused by an abortive attempt of the cell to re-enter or pass through the mitotic cycle. Therefore, agents which prevent such entry or passage are effective in preventing, or at least delaying, apoptotic cell death and are therefore useful in the treatment of neurodegenerative diseases in general, including stroke, **Alzheimer**'s disease, Parkinson's disease and motor-neuron disease in particular. Serotonin, dopamine, ascorbic acid, caffeine, hydrocortisone, and dexamethasone promoted survival of PC12 rat pheochromocytoma cells in conditions leading to apoptosis.

L13 ANSWER 24 OF 58 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 95161323 EMBASE
DN 1995161323
TI [Stress, circadian rhythms and NK cell activity].
STRESS, RITMI CIRCADIANI E ATTIVITA NK.
AU Angeli A.; Masera R.G.; Griot G.
CS Cattedra di Medicina Interna, Div. Univ. di Clinica Medica Gen., Ospedale San Luigi Gonzaga, Regione Gonzole 10,10043 Orbassano, Italy
SO Giornale di Gerontologia, (1994) 42/9 (663-666).
ISSN: 0017-0305 CODEN: GIGEAU
CY Italy
DT Journal; Conference Article
FS 003 Endocrinology
008 Neurology and Neurosurgery
037 Drug Literature Index
LA Italian
SL Italian; English
AB One prominent feature of the stress reaction is the activation of the hypothalamic-pituitary-adrenal (HPA) axis. Two hypothalamic peptides relevant to such activation have been extensively studied: corticotropin releasing hormone (CRH) and vasopressin (AVP). The activity of HPA axis is characterized by intermittent secretory bursts; episodic secretion, however, does not override a fundamental circadian program. Cortisol is generally considered an endogenous synchronizer: it gains synchronization of the human temporal structure at different levels, i.e. metabolic,

nervous and immune activities. Hypercortisolism following chronic stress may have desynchronizing effects on rhythmic immune functions. Natural killer (NK) cells are CD3-CD16+CD56+ cytotoxic lymphocytes involved in the immunosurveillance network against viruses and cancer. Cytokine and hormones are influencial on NK cell activity. We demonstrated that among HPA hormones, **cortisol** and CRH **inhibit** NK cytotoxicity, whereas ACTH and .beta.-endorphin are positive modulators. Interestingly, we documented that both the spontaneous NK activity and the responsiveness to modifiers oscillate throughout the 24-h cycle, according to circadian patterns. Maximal levels of spontaneous and cytokine-inducible NK cytotoxicity are located at the end of the night or in the early morning, whereas the susceptibility to **cortisol inhibition** reaches its peak at midnight, being phase-shiffed with respect to the spontaneous activity. We also obtained evidence that melatonin modulates NK cell activity. Although uneffective in vitro, the pineal hormone enhances the spontaneous and cytokine induced NK cytotoxicity when administered in vivo in late afternoon. No information is available about circadian variations of NK cell activity and the in vitro susceptibility to modifiers in the elderly. Our recent data suggest that **cortisol**-dependent **inhibition** is reduced in the elderly, with even lower inhibition in **Alzheimer**'s disease. These data are compatible with the concept that a peripheral glucocorticoid resistance develops with advancing age and/or mental deterioration.

L13 ANSWER 25 OF 58 CA COPYRIGHT 1999 ACS
AN 121:195782 CA
TI The role of corticosteroids in the acquisition of sensitization to locomotor stimulant effects of MK-801
AU Wedzony, Krzysztof; Czyrak, Anna
CS Institute of Pharmacology, Polish Academy of Sciences, 12 Smetna Street, Krakow, 31-343, Pol.
SO Brain Res. (1994), 657(1-2), 351-6
CODEN: BRREAP; ISSN: 0006-8993
DT Journal
LA English
AB In the present study, we investigated the role of corticosterone and glucocorticoid receptors in the acquisition of sensitization to locomotor stimulant effects of MK-801 in rats. MK-801 (two doses, 0.4 mg/kg i.p. each, given twice, 48 h apart) evoked sensitization, obsd. as enhancement of the locomotor activity to a challenging dose of MK-801 (0.4 mg/kg) but not of a stereotypy-like activity. Pharmacol. manipulations which deplete endogenous corticosterone, i.e., administration of the corticosterone synthesis inhibitor metyrapone (two injections, 150 and 50 mg/kg, given at 24 and 2 h before the first injection of MK-801, 4 mg/kg) or **blockade** of **glucocorticoid** receptors by administration of the **antiglucocorticoid** RU 38486 (20 mg/kg, 45 min before MK-801, 0.4 mg/kg) abolished the acquisition of sensitization. Thus, endogenous corticosterone and glucocorticoid receptors (type II) are involved in the acquisition of sensitization to locomotor stimulant effects of MK-801. Final expts. showed that MK-801 in doses used in the present study (0.4 mg/kg) enhanced the plasma concn. of corticosterone and that single injection of exogenous corticosterone (10 mg/kg s.c.) enhanced the locomotor stimulant effects of MK-801 (0.2 mg/kg). The obtained data indicate that the acquisition of sensitization to locomotor stimulant effects of MK-801 involves secretion of corticosteroids which probably act through glucocorticoid receptors, as was found previously for amphetamine

and its congeners.

L13 ANSWER 26 OF 58 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1994:420325 BIOSIS
DN PREV199497433325
TI **Alzheimer**-like pathology produced by sodium azide-induced cytochrome oxidase **inhibition**: Potentiation by **glucocorticoid**.
AU Bennett, M. C. (1); Mlady, G. W.; Lehman, J. C.; Rose, G. M.
CS (1) Natl. Inst. Aging, NIH, Bethesda, MD 20892 USA
SO Neurobiology of Aging, (1994) Vol. 15, No. SUPPL. 1, pp. S15.
Meeting Info.: Fourth International Conference on Alzheimer's Disease and Related Disorders Minneapolis, Minnesota, USA July 29-August 3, 1994
ISSN: 0197-4580.
DT Conference
LA English

L13 ANSWER 27 OF 58 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1994-44788 DRUGU T E
TI **Cortisol** synthesis **inhibition**: a new treatment strategy for depression.
AU Thakore J H; Dinan T G
LO London, United Kingdom
SO J.Psychopharmacol.(Oxford) (Conf.Abstr., A50, 1994)
CODEN: JOPSEQ ISSN: 0269-8811
AV St. Bartholomew's Hospital, London EC1A 7BE, England.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB Using the **cortisol** synthesis **inhibitor**, ketoconazole (KET), the Authors investigated the effects of directly lowering cortisol on the symptoms and the response of prolactin (PRL) to d-fenfluramine (D-FEN) in 8 patients suffering from major depression. PRL responses to D-FEN were measured and the patients were treated with 400-600 mg of KET for 4 wk after which they were retested. 5 Patients treated with KET recovered from their depression while the other 3 had decreases in their HAMD scores of 50% or less and were deemed partial responders. Post-treatment PRL responses to D-FEN were higher than pretreatment (57.6 +/- 2.5 vs. 129.9 +/- 9.7 mU/l). The findings imply that hypercortisolemia may be responsible for the clinical features and serotoninergic subsensitivity observed in depression. (conference abstract). (No EX).

L13 ANSWER 28 OF 58 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1993-26062 DRUGU T S E
TI Ketoconazole Administration in Hypercortisolemic Depression.
AU Wolkowitz O M; Reus V I; Manfredi F; Ingbar J; Brizendine L; Weingartner H
LO San Francisco, California, Kansas City, Kansas, Bethesda, Maryland, United States
SO Am.J.Psychiatry (150, No. 5, 810-12, 1993) 1 Tab. 16 Ref.
CODEN: AJPSAO ISSN: 0002-953X
AV Langley Porter Psychiatric Institute, 401 Parnassus Ave., San Francisco, CA 94143-0984, U.S.A.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB P.o. ketoconazole (KC, Janssen) decreased serum cortisol and depression rating scale scores when received open-label by 10 patients with major depression and hypercortisolemia. The cortisol decrease correlated with the decrease in 1 depression scale score. There were mild reversible

increases in liver function values. 2 Patients withdrew with side-effects (headache, nausea, vomiting, menstrual clotting); these patients and 1 who withdrew with an upper RTI had been receiving 1 or more of bupropion, carbamazepine, tranylcypromine and levothyroxine. KC and similar drugs might be used to investigate whether hypercortisolemia contributes to depressive symptoms. Positive results might warrant development of safer **antiglucocorticoid** drugs as antidepressant agents.

L13 ANSWER 29 OF 58 CA COPYRIGHT 1999 ACS DUPLICATE 10
AN 119:201103 CA
TI Cerebrospinal fluid corticotropin-releasing hormone and ACTH, and peripherally circulating choline-containing phospholipid in senile dementia
AU Suemaru, Shuso; Suemaru, Kohso; Hashimoto, Kozo; Ogasa, Takashi; Hirasawa, Ryuto; Makino, Shinya; Kageyama, Jingo
CS Dep. Geriatric Psychiatry Psychoneuronendocrinol., Fukuyama Yuai Hosp., Fukuyama, 720, Japan
SO Life Sci. (1993), 53(9), 697-706
CODEN: LIFSAK; ISSN: 0024-3205
DT Journal
LA English
AB Cerebrospinal fluid (CSF) levels of ACTH-releasing hormone (CRH) and ACTH, plasma levels of ACTH and cortisol, and serum levels of phospholipid and its fractions were detd. in samples taken simultaneously from patients with senile dementia of the **Alzheimer** type (SDAT), multi-infarct dementia (MID) or dementia following a cerebrovascular accident (CVD), and the borderline-to-normal control subjects. CRH levels in CSF were significantly reduced in patients with SDAT and CVD but not with MID compared to the borderline-to-normal controls. ACTH levels in CSF were significantly reduced in SDAT compared to MID. The levels of circulating lecithin (phosphatidylcholine) were depressed in a similar fashion to the levels of CRH in CSF in the SDAT patients and the group of severe dementia. Dementia and its severity did not affect the morning plasma levels of ACTH and cortisol. CSF CRH was pos. correlated with CSF ACTH, while CSF ACTH was neg. correlated with the plasma cortisol. No significant correlations were found between serum lecithin and CSF CRH or ACTH. These findings suggest that: 1) abnormalities in the extrahypothalamic CRH system play a role in the pathophysiol. of senile dementia, which may not be specific to SDAT; 2) the CRH system and the ACTH system correlate with each other within the brain; 3) CSF ACTH is subject to the feedback **inhibition** by circulating **cortisol**; and 4) in the SDAT patients and the severe dementia group CSF CRH and serum lecithin are reduced probably via independent mechanisms.

L13 ANSWER 30 OF 58 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1994:117372 BIOSIS
DN PREV199497130372
TI The pathophysiologic significance of hyperadrenocorticism: **Antiglucocorticoid** strategies.
AU Murphy, Beverley E. P. (1); Wolkowitz, Owen M.
CS (1) Montreal General Hospital, 1650 Cedar, Montreal, PQ H3G 1A4 Canada
SO Psychiatric Annals, (1993) Vol. 23, No. 12, pp. 682-690.
ISSN: 0048-5713.
DT General Review
LA English

L13 ANSWER 31 OF 58 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1993-51797 DRUGU P E
TI oCRH and Metyrapone Challenge in Cushing's Disease Patients With and Without Depressed Mood.

AU Starkman M N; Schteingart D E; Schork M A
LO Ann Arbor, Michigan, United States
SO Neuropsychopharmacology (9, No. 2, Suppl., 109S, 1993)
CODEN: NEROEW ISSN: 0893-133X
AV Department of Psychiatry, University of Michigan Medical School, 1500 East Medical Center Drive, Ann Arbor, MI 48109-0840, U.S.A.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB The hypothesis that Cushing's disease patients (CD) with depressed mood (DM) would show a reduced ACTH response to ovine corticoliberin (oCRH) compared to CD patients without DM was tested. The ACTH response to metyrapone (MP) was also studied in depressed compared to non-depressed CD patients. Comparing the 2 subgroups of 8 CD patients, patients with DM demonstrated a reduced ACTH response to 2 different secretory stimuli:
oCRH, and the sustained **block** of **cortisol** synthesis
by MP. (congress abstract).

L13 ANSWER 32 OF 58 CA COPYRIGHT 1999 ACS DUPLICATE 11
AN 119:6413 CA
TI Age and sex differences of dehydroepiandrosterone sulfate (DHEAS) and cortisol (CRT) plasma levels in normal controls and **Alzheimer**'s disease (AD)
AU Leblhuber, F.; Neubauer, C.; Peichl, Marianne; Reisecker, F.; Steinparz, F. X.; Windhager, E.; Dienstl, Elisabeth
CS Dep. Gerontol., Wagner-Jauregg-Krankenhaus, Linz, A-4020, Austria
SO Psychopharmacology (Berlin) (1993), 111(1), 23-6
CODEN: PSCHDL; ISSN: 0033-3158
DT Journal
LA English
AB DHEAS and CRT blood plasma levels were studied in 50 healthy subjects and 24 patients with **Alzheimer** disease (AD). In normal subjects there was a clear neg. correlation of DHEAS with age, while no significant age-correlated decrease of CRT levels was found. There was a decrease in the DHEAS/CRT ratio in elderly controls aged >60 yr as compared to young individuals <45 yr. There was a trend to lower DHEAS/CRT ratios in AD patients compared to age matched controls; there was a decrease of this ratio in female AD patients compared to age matched female controls, but there was none in male **Alzheimer** patients. There was a difference in CRT plasma levels between female AD patients and age matched female controls and between female and male AD patients. Considering the **antiglucocorticoid** effects of DHEAS, this ratio may account for the DHEAS protective effect against brain hippocampal degeneration caused by glucocorticoids and possibly for the higher rate of AD in females.

L13 ANSWER 33 OF 58 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1993-31040 DRUGU T S
TI Clinical Management of the Depressed Geriatric Patient: Current Therapeutic Options.
AU Mendels J
LO Philadelphia, Pennsylvania, United States
SO Am.J.Med. (94, No. 5A, 13S-18S, 1993) 3 Fig. 3 Tab. 26 Ref.
CODEN: AJMEAZ ISSN: 0002-9343
AV Philadelphia Medical Institute, 1015 Chestnut Street, Philadelphia, Pennsylvania 19096, U.S.A.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB Current therapeutic drug options for the depressed geriatric patient are reviewed with special reference to the clinical efficacies and adverse

reaction liabilities of tricyclic antidepressants (TCA), MAOI and selective 5-HT reuptake inhibitors (SSRI). Although all these drug classes are effective antidepressants, SSRI appear to be safer and to have a wider therapeutic index than either TCA or MAOI. Among SSRI, sertraline (SE) is particularly well suited to treating the elderly depressive. Atypical antidepressants appear to be poorly suited to this end. Nonpharmacological management options include **psychotherapy** and ECT. Drugs which can precipitate depression in the elderly are also mentioned. (congress).

L13 ANSWER 34 OF 58 MEDLINE
AN 92343930 MEDLINE
DN 92343930
TI **Antiglucocorticoid** effects of DHEA-S in **Alzheimer**'s disease [letter] [published erratum appears in Am J Psychiatry 1992 Nov;149(11):1622] [comment] [see comments].
CM Comment on: Am J Psychiatry 1990 Oct;147(10):1297-303
Comment in: Am J Psychiatry 1993 Sep;150(9):1432-3
AU Leblhuber F; Windhager E; Neubauer C; Weber J; Reisecker F; Dienstl E
SO AMERICAN JOURNAL OF PSYCHIATRY, (1992 Aug) 149 (8) 1125-6.
Journal code: 3VG. ISSN: 0002-953X.
CY United States
DT Commentary
Letter
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199210

L13 ANSWER 35 OF 58 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 92328715 EMBASE
DN 1992328715
TI Erratum: **Antiglucocorticoid** effects of DHEA-S in **Alzheimer**'s disease (American Journal of Psychiatry (Aug 1992) (1126)).
AU Wolkowitz O.M.
SO American Journal of Psychiatry, (1992) 149/11 (1622).
ISSN: 0002-953X CODEN: AJPSAO
CY United States
DT Journal; Errata
FS 030 Pharmacology
LA English

L13 ANSWER 36 OF 58 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 92242938 EMBASE
DN 1992242938
TI **Antiglucocorticoid** effects of DHEA-S in **Alzheimer**'s disease [17].
AU Leblhuber F.; Windhager E.; Neubauer C.; Weber J.; Reisecker F.; Dienstl E.; Wolkowitz O.M.; Reus V.I.; Manfredi F.; Roberts E.
SO American Journal of Psychiatry, (1992) 149/8 (1125-1126).
ISSN: 0002-953X CODEN: AJPSAO
CY United States
DT Journal; Letter
FS 032 Psychiatry
037 Drug Literature Index
LA English

L13 ANSWER 37 OF 58 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1992-25751 DRUGU P S E
TI The Overnight Metyrapone Test is the Procedure of Choice in Screening for
Adrenal Insufficiency.
AU Kirby J; Cunningham S; McKenna T J
LO Dublin, Eire,
SO J.Endocrinol. (132, Suppl., 109, 1992)

CODEN: JOENAK ISSN: 0892-7790
AV Department of Endocrinology and Diabetes Mellitus, St. Vincent's Hospital, Elm Park, Dublin, Eire.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB This study was designed to examine the performance of the overnight metyrapone test (OMT) which tests the entire hypothalamic-pituitary-adrenal axis (HPAA). Measurements of 11-deoxycortisol (cortodoxone), ACTH, cortisol (hydrocortisone) and the cortisol response to hypoglycemia were examined. The responses to 323 OMT were analyzed; 229 were normal and 94 were subnormal. 1 Subject complained of vomiting and 1 had alarmingly vivid dreams but no subject experienced worsening of symptoms of adrenal insufficiency. Results indicate that the OMT is a safe, convenient and sensitive test of function in the HPAA and is therefore recommended as the procedure of choice when screening for adrenal insufficiency. (congress abstract).

L13 ANSWER 38 OF 58 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1993:146550 BIOSIS
DN PREV199395079350
TI Psychoimmunoendocrine aspects of panic disorder.
AU Brambilla, F. L. Bellodi (1); Perna, G.; Battaglia, M.; Sciuto, G.; Diaferia, G.; Petraglia, F.; Panerai, A.; Sacerdote, P.
CS (1) Centro di Psiconeuroendocrinologia, Ospedale Psichiatrico Pini, Via Ippocarate 45, I-Milano 20161 Italy
SO Neuropsychobiology, (1992) Vol. 26, No. 1-2, pp. 12-22.
ISSN: 0302-282X.
DT Article
LA English
AB Immunological, neuroendocrine and psychological parameters were examined in 14 psychophysically healthy subjects and in 17 panic disorder patients before and after a 30-day course of alprazolam therapy. T lymphocyte proliferation in response to the mitogen phytohemoagglutinin, lymphocyte beta-endorphin (beta-EP) concentrations, plasma ACTH, cortisol and beta-EP levels were examined in basal conditions and after corticotropin-releasing hormone (CRH) stimulation. **Cortisol inhibition** by dexamethasone (DST) and basal growth hormone, (GH) and prolactin levels were also examined. Depression, state or trait anxiety, anticipatory anxiety, agoraphobia, simple and social phobias, severity and frequency of panic attacks were monitored by rating scales. The immune study did not reveal any significant difference between patients and controls, or any effect of alprazolam therapy. The hormonal data for the two groups were similar, except for higher than normal basal ACTH and GH plasma levels, lower than normal ratios between the ACTH and cortisol respones to CRH, and blunted DST in some patients. All the impairments improved after alprazolam therapy, in parallel with decreases in anxiety and in severity and frequency of panic attacks.

L13 ANSWER 39 OF 58 CA COPYRIGHT 1999 ACS
AN 115:107142 CA
TI Regulation of nerve growth factor synthesis in the central nervous system for neurological disease treatment
IN Lindholm, Dan Bjarne; Thoenen, Hans Friedrich Erwin; Hengerer, Bastian
PA Max-Planck-Gesellschaft zur Foerderung der Wissenschaften e.V., Fed. Rep. Ger.
SO PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DT Patent
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9102067	A1	19910221	WO 1990-EP1232	19900727
	RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
	EP 484416	A1	19920513	EP 1990-911746	19900727
	R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
	JP 05025056	A2	19930202	JP 1990-198053	19900727
PRAI	US 1989-386546	19890727			
	US 1990-555006	19900720			
	WO 1990-EP1232	19900727			

AB A method is provided for regulating levels of nerve growth factor (NGF) in the central nervous system, and is based on the discovery that in vivo synthesis of NGF may be regulated by various cytokines. The regulation may be achieved by administering an effective amt. of a cytokine or an effective amt. of a substance which alters the levels of a cytokine [e.g. a **glucocorticoid inhibitor** of interleukin-1 (IL-1)]. Alternatively, the NGF promoter may be linked to a nucleic acid sequence encoding a protein or peptide of interest (e.g. a neurotrophic factor) and the transcription of the protein or peptide of interest may be controlled by exposing the NGF promoter to a substance which regulates the expression of NGF. Thus, IL-1.beta. increased NGF mRNA .apprx.5-fold, basic fibroblast growth factor and epidermal growth factor increased NGF mRNA .apprx.7-fold, and transforming growth factor-.alpha. (TGF-.alpha.) increased NGF mRNA .apprx.9-fold in cultured astrocytes. IL-1.beta. and TGF-.beta.1 increased NGF mRNA in the hippocampus 4-5-fold and 3-4-fold, resp. Using sciatic fibroblasts transfected with a construct contg. the NGF promoter and a chloramphenicol acetyltransferase reporter gene, the glucocorticoid dexamethasone was found to neg. regulate NGF expression at the gene level. TGF-.beta.1 increased transcription of the NGF gene.

L13 ANSWER 40 OF 58 BIOSIS COPYRIGHT 1999 BIOSIS
AN 1991:301108 BIOSIS
DN BA92:22123
TI NEUROENDOCRINE PHYSIOLOGIC AND BEHAVIORAL RESPONSES FOLLOWING INTRAVENOUS NICOTINE IN NONSMOKING HEALTHY VOLUNTEERS AND IN PATIENTS WITH **ALZHEIMER**'S DISEASE.
AU NEWHOUSE P A; SUNDERLAND T; NARANG P K; MELLOW A M; FERTIG J B; LAWLOR B A; MURPHY D L
CS NEUROSCI. RES. UNIT, DEP. PSYCHIATRY, UNIV. VT. COLL. MED., 1 SOUTH PROSPECT ST., BURLINGTON, VT. 05401.
SO PSYCHONEUROENDOCRINOLOGY, (1990 (1991)) 15 (5-6), 471-484.
CODEN: PSYCDE. ISSN: 0306-4530.
FS BA; OLD
LA English
AB In separate studies, nonsmoking nicotine-naive subjects (11 young and middle-aged normal volunteers and 11 nonsmoking patients with **Alzheimer**'s disease) received up to three doses of intravenous nicotine bitartrate (0.125, 0.25, and 0.5 .mu.g/kg/min) and placebo for 60 min. Measurement of plasma ACTH, cortisol, and prolactin showed that nicotine produced in both groups a dose-dependent increase in cortisol, with ACTH in both groups and prolactin in the **Alzheimer**'s group significantly elevated only by the 0.5 .mu.g dose. Physiologic measures showed dose-dependent increases that were consistent with previous reports of nicotinic cholinergic stimulation. Behavioral effects included increases in anxiety and decreases in mood, especially following the 0.5 .mu.g dose. Physical side effects were modest. The results indicate that nicotinic cholinergic stimulation can activate pituitary hormonal secretion in the human and suggest that nicotinic cholinergic stimulation may constitute an important part of cholinesterase inhibitor-induced

endocrine stimulation and behavioral activation.

L13 ANSWER 41 OF 58 BIOSIS COPYRIGHT 1999 BIOSIS DUPLICATE 12
AN 1991:277194 BIOSIS
DN BA92:9809
TI CIRCADIAN AND SLEEP-RELATED ENDOCRINE RHYTHMS IN **SCHIZOPHRENIA**.
AU VAN CAUTER E; LINKOWSKI P; KERKHOFS M; HUBAIN P; L'HERMITE-BALERIAUX M; LECLERCQ R; BRASSEUR M; COPINSCHI G; MENDLEWICZ J
CS DEP. MED., BOX 138, UNIV. CHICAGO, 5841 S. MARYLAND AVE., CHICAGO, ILL. 60637.
SO ARCH GEN PSYCHIATRY, (1991) 48 (4), 348-356.
CODEN: ARGPAQ. ISSN: 0003-990X.
FS BA; OLD
LA English
AB Plasma levels of prolactin, growth hormone, corticotropin, and cortisol were measured at 15-minute intervals for 24 hours in nine unmedicated male **schizophrenic** patients and in nine age-matched normal male subjects. Each study was preceded by 3 days of habituation to the laboratory environment. Sleep was polygraphically recorded. The circadian and pulsatile variations present in each hormonal profile were quantitatively characterized with the use of computer algorithms specifically designed for analyses of hormonal fluctuations. The major abnormality of neuroendocrine release that was observed in the **schizophrenic** patients was an almost threefold enhancement of the sleep-related increase in the prolactin level, associated with an intensified frequency of nocturnal prolactin pulses. This increased stimulatory effect of sleep on prolactin secretion was evident immediately after sleep onset. The normal **inhibition** of **cortisol** secretion during early sleep was absent in **schizophrenic** patients. The major sleep abnormalities were a prolonged sleep latency and a reduction in total rapid eye movement stage sleep. During wakefulness, prolactin and cortisol levels were normal. The 24-hour profile of growth hormone was unaltered in **schizophrenic** patients, and a sleep-onset growth hormone pulse was observed in all patients. No abnormalities were noted in the levels or temporal organization of corticotropin secretion. Both the amplitude and the timing of the cortisol rhythm were normal. We conclude that, in **schizophrenic** men, pituitary-adrenal function and circadian time-keeping are normal but prolactin secretion is hyperresponsive to the physiologic stimulus of sleep onset. **Schizophrenia** thus appears to be characterized by a subset of neuroendocrine disturbances distinct from that observed in major endogenous depression.

L13 ANSWER 42 OF 58 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1991-50698 DRUGU P
TI Principles of Clinically Important Drug Interactions with Carbamazepine. Part II.
AU Ketter T A; Post R M; Worthington K
LO Bethesda, Maryland, United States
SO J.Clin.Psychopharmacol. (11, No. 5, 306-13, 1991) 159 Ref.
CODEN: JCPYDR ISSN: 0271-0749
AV Biological Psychiatry Branch, NIMH, Building 10, Room 3N212, 9000 Rockville Pike, Bethesda, MD 20892, U.S.A.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB Clinically important drug interactions with carbamazepine (CBZ) are reviewed, with reference to decreasing efficacy and causing CBZ toxicity by inhibition and induction of metabolism. Drug interactions have been

reported with **antipsychotics** such as haloperidol, anxiolytics, calcium channel blockers such as diltiazem and verapamil but not nifedipine, hypolipidemics, digoxin, **glucocorticoids**, histamine H2 **blockers**, lithium, local anesthetics, ethanol, cigarettes, caffeine, hormonal contraceptives and androgens such as danazol, chlorpropamide and diuretics, thyroid hormones and other miscellaneous drugs. Knowledge of CBZ drug interactions is essential for the safe and effective management of patients requiring medication combinations.

L13 ANSWER 43 OF 58 BIOSIS COPYRIGHT 1999 BIOSIS DUPLICATE 13
AN 1991:415873 BIOSIS
DN BA92:82838
TI COCAINE BLOCKS EXTRANEURONAL UPTAKE OF NOREPINEPHRINE BY THE PREGNANT HUMAN UTERUS.
AU HURD W W; SMITH A J; GAUVIN J M; HAYASHI R H
CS DEP. OBSTETRICS GYNECOL., UNIV. MICHIGAN MED. CENTER, ANN ARBOR, MICH. REPRINTS NOT AVAILABLE.
SO OBSTET GYNECOL, (1991) 78 (2), 249-253.
CODEN: OBGNAS. ISSN: 0029-7844.
FS BA; OLD
LA English
AB Premature labor is one of the most common complications associated with **cocaine abuse** during pregnancy. Still, the efect of cocaine on the pregnant uterus is largely unknown. Although inhibition of neuronal uptake is the most important effect of cocaine in most tissues, after mid-pregnancy, the uterus has few functioning adrenergic nerve endings. To determine whether cocaine has any effect on uptake during pregnancy, we evaluated the ability of the term pregnant human uterus to take up [3H]-norepinephrine (9 .times. 10-8 mol/L) and the ability of cocaine (10-6-10-8 mol/L) to block this uptake. Because d-propranolol has been shown to block the direct effects of cocaine on the pregnant rabbit uterus, we also evaluated the ability of d-propranolol (2 .times. 10-6 mol/L) to block the effect of cocaine on catecholamine uptake. The ability of the Uptake 2 **inhibitor hydrocortisone** (2 .times. 10-5 mol/L) to block catecholamine uptake was also studied. We found that [3H]-norepinephrine was taken up by both the pregnant myometrium and endometrium, and that cocaine blocked this uptake by up to 55% at concentrations as low as 10-7 mol/L. D-propranolol had no effect on the ability of cocaine to **block** catecholamine uptake. **Hydrocortisone blocked** uptake by the endometrium by 15% but did not block uptake by the myometrium. We conclude that the pregnant human uterus at term retains the ability to take up catecholamines and that cocaine blocks this extraneuronal uptake. This may explain, in part, the association of cocaine use with premature labor.

L13 ANSWER 44 OF 58 MEDLINE
AN 92040606 MEDLINE
DN 92040606
TI Resistance of beta-endorphin to dexamethasone inhibition in Parkinson's and **Alzheimer**'s diseases.
AU Airaghi L; Catania A; Gramigna C; Manfredi M G; Franceschi M; Zanussi C
CS 1st Medical Clinic, University of Milan, Italy.
SO INTERNATIONAL JOURNAL OF NEUROSCIENCE, (1991 Jan-Feb) 56 (1-4) 73-9.
Journal code: GS4. ISSN: 0020-7454.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199202
AB The response of plasma beta-endorphin (beta-EP) to dexamethasone suppression was studied in 14 patients with **Alzheimer**'s disease (AD), 14 patients with Parkinson's disease (PD), and 13 age-matched controls in order to evaluate whether an impairment of the opiate system

is present in these neurodegenerative disorders. Basal circulating beta-EP
was in normal range in all subjects, although the mean concentration was slightly reduced in the patients compared to controls. After 1 mg dexamethasone given at 11:00 p.m. the night before, plasma beta-EP concentration measured at 08:00 a.m. and 04:00 p.m. was not inhibited in AD and PD patients while it was significantly reduced in controls. Circulating ACTH and cortisol were similar in patients and controls and a normal **inhibition** of plasma **cortisol** after
dexamethasone was observed in 13/14 AD and 12/14 PD patients. The resistance of beta-EP to dexamethasone inhibition is consistent with previous clinical and experimental data indicating a disorder of the opiate system in brain degenerative diseases.

L13 ANSWER 45 OF 58 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1991-13449 DRUGU T S
TI Treatment of **Alzheimer**'s Disease with Cholinergic Drugs.
AU Kumar V; Calache M
LO Springfield, Illinois, United States
SO Int.J.Clin.Pharmacol.Ther.Toxicol. (29, No. 1, 23-37, 1991) 4 Tab. 96 Ref.
CODEN: IJCPB5 ISSN: 0174-4879
AV S.I.U. School of Medicine, P.O. Box 19230, Springfield, IL 62794-9230, U.S.A.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB The review considers several cholinergic drugs that have been tried in patients with **Alzheimer**'s disease (AD), including choline, lecithin, physostigmine, metrifonate, tacrine, arecoline, oxtremorine, bethanecol and RS-86. Unfortunately, results have been somewhat disappointing, and none of these agents are free of side-effects. Experience may indicate that cholinergic agents alone may not be sufficient to produce cognitive improvement in AD, and there seems to be a need to develop drugs which could affect several neurotransmitter systems. Neuroendocrine changes induced by these drugs may be useful as biological markers in estimating their central effects.

L13 ANSWER 46 OF 58 MEDLINE DUPLICATE 14
AN 90242014 MEDLINE
DN 90242014
TI Hypercortisolism and its possible neural bases.
AU Sapolsky R M; Plotsky P M
CS Department of Biological Sciences, Stanford University, California 94305-5020.
NC R01 AG06633 (NIA)
R01 DK33093 (NIDDK)
SO BIOLOGICAL PSYCHIATRY, (1990 May 1) 27 (9) 937-52. Ref: 95
Journal code: A3S. ISSN: 0006-3223.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199008
AB As is clear from the pages of this journal, biological psychiatrists remain fascinated by the phenomenon of dexamethasone (DEX) resistance and the hypercortisolism of various neuropsychiatric disorders. The mere existence of the endocrine abnormalities attests to the biological reality
of these disorders. Furthermore, progress continues in using the occurrence of these endocrine defects as both diagnostic and prognostic markers of disease subtypes. Progress has also been made in understanding

the mechanisms underlying the endocrine defects. The adrenocortical axis is vastly complex, involving multiple hypothalamic-releasing factors under CNS control, shifting pituitary and adrenal sensitivies to hormonal signals, and feedback regulation at all three levels. What defects within this system produce DEX resistance and hypercortisolism? In this paper, we review data suggesting that the endocrine problems is, at least in part, neural in nature. Drawing upon a rodent literature, we will also suggest some models by which this can occur. The hypercortisolism found in cases of affective disorders, anorexia nervosa, **Alzheimer**'s disease, among the very aged or the chronically stressed, is not a uniform phenomenon. Basal cortisol concentrations can be elevated in all or part of the circadian cycle. Resistance to **glucocorticoid** (GC) feedback **inhibition** (as typically demonstrated by DEX resistance) can occur; the resistance can be complete, or occur as early escape from DEX suppression. Finally, elevated basal cortisol concentrations and DEX resistance can occur independently of each other. Until the end of this review, we will conveniently refer to these variants of adrenocortical hyperactivity as "hypercortisolism." In addition, rather than using the term "hypercortisolism" for the rat, we will use "hyperadrenocorticism" (as they secrete corticosterone, rather than cortisol).

L13 ANSWER 47 OF 58 BIOSIS COPYRIGHT 1999 BIOSIS DUPLICATE 15
AN 1990:499502 BIOSIS
DN BA90:127848
TI STRESS-ADAPTATION FAILURE HYPOTHESIS OF **ALZHEIMER**'S DISEASE.
AU DESHMUKH V D; DESHMUKH S V
CS DEP. NEUROL., UNIV. FLA., UNIV. HOSP., 655 WEST EIGHTH ST., JACKSONVILLE, FLA. 32209, USA.
SO MED HYPOTHESES, (1990) 32 (4), 293-296.
CODEN: MEHYDY. ISSN: 0306-9877.
FS BA; OLD
LA English
AB It is proposed that the higher incidence of chronic stress-adaptation failure in patients with **Alzheimer**'s disease is of specific etiopathological significance. Such chronic stress-adaptation failure leads to a vicious circular reaction, namely: intense, stressful, stimuli .fwdarw. neocrotico-limbic excitation .fwdarw. hypothalamo-pituitary-adrenocortical (HPA) axis activation .fwdarw. excessive secretion of neurohormones including cortisol .fwdarw. stimulation of **inhibitory glucocorticoid** sensitive hippocampal neurons .fwdarw. failure to terminate the HPA axis response .fwdarw. chronic excessive secretion of neurohormones including cortisol .fwdarw. overstimulation degeneration of **glucocorticoid** sensitive hippocampal **inhibitory** neurons .fwdarw. progressive cognitive-affective behavioral disorganizational failure which is typical of dementia of the **Alzheimer**'s type. Possibilities of neuropharmacological corrections and neurobehavioral re-education are suggested.

L13 ANSWER 48 OF 58 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1990-37608 DRUGU P T
TI Physiological Effects of Acetyl-Levo-Carnitine in the Central Nervous System.
AU Bodis Wollner I
LO New York, New York, United States
SO Int.J.Clin.Pharmacol.Res. (10, No. 1-2, 109-14, 1990) 29 Ref.
CODEN: CPHRDE ISSN: 0251-1649
AV The Visual Evoked Potentials Laboratory, Department of Neurology, The Mount Sinai Medical Center, New York, N.Y., U.S.A.
LA English

DT Journal
FA AB; LA; CT
FS Literature
AB Electrophysiological and neurophysiological effects of acetyl-L-carnitine
(ALC) in CNS are reviewed with reference both to its effects on P300 (an event-related cortical EEG potential) in monkey models of cognitive dysfunction and to its potential therapeutic value against parkinsonism and other dementing illnesses, particularly in elderly patients. (congress).

L13 ANSWER 49 OF 58 MEDLINE
AN 90081061 MEDLINE
DN 90081061
TI **Antiglucocorticoid** actions of dehydroepiandrosterone and low concentrations in **Alzheimer**'s disease [letter; comment].
CM Comment on: Lancet 1989 Sep 9;2(8663):577-80
AU Svec F; Lopez A
SO LANCET, (1989 Dec 2) 2 (8675) 1335-6.
Journal code: L0S. ISSN: 0140-6736.
CY ENGLAND: United Kingdom
DT Commentary
Letter
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 199003

L13 ANSWER 50 OF 58 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 90005887 EMBASE
DN 1990005887
TI **Antiglucocorticoid** actions of dehydroepiandrosterone and low concentrations in **Alzheimer**'s disease.
AU Svec F.; Lopez -S.A.
CS Section of Endocrinology, Department of Medicine, Louisiana State University Medical Center, New Orleans, LA 70112, United States
SO Lancet, (1989) 2/8675 (1335-1336).
ISSN: 0140-6736 CODEN: LANCAO
CY United Kingdom
DT Journal; Letter
FS 003 Endocrinology
005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery
020 Gerontology and Geriatrics
021 Developmental Biology and Teratology
LA English

L13 ANSWER 51 OF 58 CA COPYRIGHT 1999 ACS
AN 110:128523 CA
TI Effect of phenothiazine **psychotropics** on template activity of thymocyte DNA and glucocorticoid receptor interaction
AU Golikov, P. P.
CS N. V. Sklifosovskii Inst. Emergency Aid, Moscow, USSR
SO Byull. Eksp. Biol. Med. (1989), 107(1), 56-8
CODEN: BEBMAE; ISSN: 0365-9615
DT Journal
LA Russian
AB Studies in adrenalectomized rats indicate that the ability of aminazine and tisercin to suppress DNA template activity ([3H]uridine incorporation into mRNA) in thymocytes is mediated by their action on type II glucocorticoid receptors.

L13 ANSWER 52 OF 58 BIOSIS COPYRIGHT 1999 BIOSIS DUPLICATE 16
AN 1989:32207 BIOSIS
DN BA87:20207
TI CORTISOL RESPONSES TO CHOLINERGIC DRUGS IN **ALZHEIMER**'S DISEASE.

AU KUMAR V; SMITH R C; SHERMAN K A; ASHFORD W; MURPHY J; GIACOBINI E; COLLIVER J
CS DEP. PSYCHIATRY, SOUTH. ILL. UNIV. SCH. MED., P.O. BOX 19230, SPRINGFIELD, ILL. 62794-9230, USA.
SO INT J CLIN PHARMACOL THER TOXICOL, (1988) 26 (10), 471-476. CODEN: IJCPB5. ISSN: 0300-9718.
FS BA; OLD
LA English
AB Patients with **Alzheimer**'s disease participated in a trial of two sessions in which they received physostigmine and neostigmine in a double-blind crossover disign. Most of these patients subsequently participated in a scopolamine vs saline double-blind crossover trial using a similar design. Physostigmine increased plasma cortisol relative to neostigmine, with the greatest difference at time points greater than 90 min post drug oral administration. Physostigmine also significantly decreased plasma cholinesterase (ChE). There was a significant positive correlation between the effects of physostigmine on increasing cortisol and decreasing ChE; there was no correlation between the increase in **cortisol** of cholinesterase **inhibitor** following neostigmine administration, but neither of these chemical parameters is related to the drug's effects on cognitive functioning.

L13 ANSWER 53 OF 58 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1989-00923 DRUGU P E
TI Opioidergic Regulation of Hypothalamo-Pituitary-Adrenal Function in Depression and Cushing's Disease: An Interim Report.
AU Zis A P
LO Vancouver, British Columbia, Canada
SO Psychoneuroendocrinology (13, No. 5, 419-30, 1988) 3 Tab. 78 Ref. CODEN: PSYCDE ISSN: 0306-4530
AV Department of Psychiatry, The University of British Columbia, University Hospital, UBC Site, 2255 Wesbrook Mall, Vancouver, B.C. V6T 2A1, Canada.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB The review considers the status of the hypothalamic-pituitary-adrenal axis in patients with depression and Cushing's disease, together with the role of endogenous opioids in the regulation of this system. The effects of administration of agonists such as codeine, morphine, beta-endorphin and FK-33842 and antagonists such as naloxone on plasma levels of cortisol and ACTH are considered. The evidence for the presence of an inhibitory opioid mechanism on the human hypothalamic-pituitary-adrenal axis is compelling.

L13 ANSWER 54 OF 58 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1987-50298 DRUGU P E
TI Dexamethasone Suppression Test: Usefulness of Relative Indices to Define Suppression-Nonsuppression States in Depression.
AU Olivera A A; Fero D; Scibilia J
LO Brecksville, Cleveland, Ohio, United States
SO Curr.Ther.Res. (42, No. 4, 627-32, 1987) 2 Tab. 9 Ref. CODEN: CTCEA9 ISSN: 0011-393X
AV Brecksville Veterans Administration Medical Center, Brecksville, Cleveland, Ohio, U.S.A.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB 30/201 Depressed male patients were classified as nonsuppressors by the cortisol suppression index (CSI) and the **inhibition** of **cortisol** production (ICP) after dosing with p.o. dexamethasone (DM). 12 Patients increased their sensitivity to **inhibition** of

cortisol production by DM upon treatment with the antidepressants desipramine (DP); trazodone (TZ) with or without propanolol (PP) and doxepin with or without PP. They underwent conversion to suppressor state after antidepressant treatment and were indistinguishable from untreated suppressors.

L13 ANSWER 55 OF 58 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1987-00455 DRUGU T E
TI Dexamethasone Suppression Test: Conversion of Nonsuppressor to Suppressor State by Trazodone.
AU Olivera A A; Fero D
LO Brecksville, Cleveland, Ohio, United States
SO Curr.Ther.Res. (40, No. 5, 949-52, 1986) 1 Tab. 11 Ref.
CODEN: CTCEA9 ISSN: 0011-393X
AV 10000 Brecksville, Ohio 44141, U.S.A.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB In 23 depressed patients with initial non-suppression cortisol response in the dexamethasone (p.o.) suppression test, achievement of maximal clinical improvement with trazodone (in 11 cases), doxepin (7 cases) or imipramine and desipramine (5 cases) was accompanied by conversion to suppressor status on repeat testing. No significant difference between the response in patients treated with trazodone and the response in those given doxepin or imipramine and desipramine was detected.

L13 ANSWER 56 OF 58 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1985-39940 DRUGU P E
TI Cortisol Escape from Morphine Suppression.
AU Zis A P; Haskett R F; Albala A A; Carroll B J; Lohr N E
LO Vancouver, British Columbia, Canada; Ann Arbor, Michigan, Durham, North Carolina, United States
SO Psychiatry Res. (15, No. 2, 91-95, 1985) 1 Fig. 1 Tab. 13 Ref.
CODEN: PSRSDR ISSN: 0165-1781
AV Dept. of Psychiatry, Vancouver General Hospital, 2775 Heather St., Vancouver, BC V5Z 1M9, Canada.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB In 21 psychiatric patients, early resumption of i.v. morphine sulfate (MP)-**blocked cortisol** (CS) secretion (escape) was more frequent in patients with major depressive disorders (MDD) and with abnormal dexamethasone suppression test (DST) results, than in other psychiatric patients or normal controls.

L13 ANSWER 57 OF 58 DRUGU COPYRIGHT 1999 DERWENT INFORMATION LTD
AN 1984-09940 DRUGU P S
TI **Psychotropic** Drugs and Anesthetic Management.
AU Bricard H; Moulin M; Fauchon G; Gerard J L; Hurpe J M; Tartiere J
LO Caen, France
SO Therapie (38, No. 5, 519-28, 1983) 1 Fig. 1 Tab. 52 Ref.
CODEN: THERAP ISSN: 0040-5957
AV Departement d'Anesthesie -Reanimation, C.H.U. Cote de Nacre, 14000 Caen Cedex, France.
LA French
DT Journal
FA AB; LA; CT
FS Literature
AB A review on possible interactions between various classes of **psychotropic** drugs and agents commonly used in general anesthesia

is presented. The **psychotropic** drugs mentioned were the amphetamines, monoamine oxidase inhibitors, tricyclic and other antidepressants, barbiturates, phenothiazines and benzodiazepines. General anesthetics comprised halothane, pethidine, morphine, Na nitroprusside, prostigmine etc. (congress).

L13 ANSWER 58 OF 58 EMBASE COPYRIGHT 1999 ELSEVIER SCI. B.V.
AN 82205869 EMBASE
DN 1982205869
TI Calmodulin antagonists competitively inhibit dexamethasone binding to the glucocorticoid receptor.
AU Van Bohemen C.G.; Rousseau G.G.
CS Int. Inst. Cell. Mol. Pathol., 1200 Brussels, Belgium
SO FEBS Letters, (1982) 143/1 (21-25).
CODEN: FEBLAL
CY Netherlands
DT Journal
FS 037 Drug Literature Index
029 Clinical Biochemistry
003 Endocrinology
030 Pharmacology
LA English
AB We determined whether calmodulin antagonists influence dexamethasone binding to the **glucocorticoid** receptor. The **antagonists** belonged to the class of **antipsychotic** phenothiazines, i.e., trifluoperazine (TFP), membrane-active compounds, i.e., propranolol and SKF 525A, microtubule inhibitors, i.e., vinblastine, and new calmodulin inhibitors, i.e., R 24571. We show here that the calcium effect is not prevented by such antagonists of calmodulin. However, some of these and related drugs (SKF 550 and SKF 625A) competitively inhibit the binding of dexamethasone to its receptor. TFP, the most potent inhibitor, prevents induction of tyrosine aminotransferase by dexamethasone. Thus, calmodulin inhibitors may act as **glucocorticoid antagonists**, not via calmodulin inhibition but through a direct interaction with the glucocorticoid receptor.